DEVELOPMENT OF A CLINICAL PRACTICE GUIDELINE FOR THE USE OF SUGAMMADEX

by

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As members of the DNP Project Committee, we certify that we have read the DNP Project prepared by *Timothy S. Markle*, titled *Development of a Clinical Practice Guideline for the Use of Sugammadex* and recommend that it be accepted as fulfilling the DNP Project requirement for the Degree of Doctor of Nursing Practice.

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Final approval and acceptance of this DNP Project is contingent upon the candidate's submission of the final copies of the DNP Project to the Graduate College.

I hereby certify that I have read this DNP Project prepared under my direction and recommend that it be accepted as fulfilling the DNP Project requirement.

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DEDICATION

I dedicate this DNP project to my family and friends who have been a huge support to my success. Especially to my lovely wife Emily for her continued encouragement and unwavering support.

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ABSTRACT

Ineffective reversal of neuromuscular blockade is a prevalent issue for patients recovering from anesthesia, impacting over a third of our perioperative patient populations. This issue imposes the risk of postoperative complications for perioperative patients that can lead to prolonged operating room stay, prolonged recovery room stay, unplanned re-intubations, and unwarranted intensive care admissions. There is a new reversal agent, sugamamdex, which is revolutionizing how anesthesia providers are reversing neuromuscular blockade, in that it provides more timely and effective reversal. Sugammadex has recently been approved by the Food and Drug Administration (FDA), many hospitals remain reluctant to have it available on their hospital formulary. The main purpose of this Doctor of Nursing Practice (DNP) project was to develop an evidence-based clinical practice guideline (CPG) for the regulated use of sugammadex as an alternative reversal agent, to be used by anesthesia providers at a hospital in the Phoenix area. The objective is to motivate implementation of evidence-based recommendations for sugammadex by providing a high quality guideline to key leaders of the organization to promote and implement change. The Knowledge to Action Framework was utilized as the quality improvement, conceptual framework to encourage translation of current evidence into best practices. Expert practitioners (N=4) utilized the Appraisal of Guidelines for Research & Evaluation II (AGREE II) as an assessment tool to determine the quality and applicability of the developed CPG. The CPG's overall assessment achieved a score of 96%, leading to each appraiser recommending its use without modifications. Results were disseminated to key anesthesia leaders who presented the guidelines to the pharmacy and therapeutics committee which resulted in the addition of sugammadex for use by anesthesia.

INTRODUCTION

The Centers for Disease Control and Prevention (CDC), through the National Hospital Discharge Survey, estimated that there are 51.4 million surgeries performed in the United States (US) every year (Brull & Kopman, 2017). If one conservatively estimates that 60% of these surgical procedures required general anesthesia with muscle relaxation, it would equate out to 30.8 million patients that receive neuromuscular blocking agents (NMBA) annually (Brull & Kopman, 2017). This is significant due to the incidence of residual blockade, which has been found to occur in 41% of patients that receive muscle relaxation (Naguib, Kopman, & Ensor, 2007). Residual blockade causes patients to have postoperative weakness, which leads to poor respiratory mechanics, loss of airway protective reflexes, and increase risk of complications. It is conservatively estimated that one-third of all surgical patients will experience some degree of postoperative weakness, which would result in 10.1 million patients experiencing prolonged paralysis and an increased risk of postoperative complications annually in the US (Brull & Kopman, 2017). Further, 0.8% of all surgical patients will have a serious postoperative respiratory complication amounting to 81,417 patients every year in the US (Brull & Kopman, 2017). This has led to an increased emphasis on measures to enhance both effective monitoring and reversal of neuromuscular blockade. One way to address this issue is through the development of a clinical practice guideline (CPG), which includes evidence based research to guide practice.

CPGs provide recommendations driven by published research. This minimizes ineffective patient care, and reduces the variety of care from different healthcare organizations (Tymkow, 2011). There has been an extensive push for healthcare professionals to attain new knowledge

and adapt their clinical care to current best practices, which is known as evidence-based practice (EBP). EBP intertwines the currently best available research in the literature with clinical expertise to result in enhanced patient care (Zaccagnini & White, 2011). The DNP prepared advanced practice nurse (APRN) has many roles, including identifying gaps in knowledge and propel the implementation of EBP in all aspects of healthcare, such as the incorporation of CPGs into practice. There is a current EBP lag in healthcare organizations related to the fear of change to 'how it has always been done' or the status quo, which can lead to inappropriate patient care. The transition of information into policies has been found to have a lag time of eight to fifteen years, which highlights the need for enhanced provider education and guidelines that evolve with research (Dobbins, Ciliska, Estabrooks, & Hayward, 2005). This ineffective evolution of best-practice is only found to be more astonishing when it takes numerous years for the development of CPGs from current literature recommendations. DNP providers can promote best practice by ensuring that CPGs are developed from evidence-based recommendations and continually evolve with the current literature.

Background Knowledge

Ineffective reversal of neuromuscular blockade may lead to prolonged paralysis and weakness of surgical patients whom have been administered NMBAs. This is known as postoperative residual curarization (PORC), which can lead to respiratory insufficiency, hypoxemia, and even death if unnoticed. PORC has become a highly prevalent issue in our healthcare organizations for surgical patients recovering from anesthesia whom received NMBA intraoperatively by decreasing surgical patients' ability to protect their own airway and ventilate adequately. This becomes a serious consideration for providers in the US due to the majority of

cases, up to 60%, are being performed as outpatient, single-day cases, in which patients are being sent home with NMBAs still affecting their neuromuscular junctions (Farhan, Moreno-Duarte, McLean, & Eikermann, 2014). Effective muscle relaxation is a critical component of providing exceptional anesthesia for tracheal intubation and maintaining surgical exposure, however it does require a delicate balance due to the potential for inadequate recovery from anesthesia and recurarization. Anesthesia providers employ just enough medication to adequately anesthetize and paralyze (render immobile) intraoperative patients for surgical procedures, while maintaining the capability of patients to safely and rapidly recover from anesthesia at the end of the case.

The prevalence of recurarization in the postoperative phase has been reported by numerous meta-analyses to be anywhere from 38 to 41% of surgical patients (Farhan et al., 2014; Naguib, Kopman, & Esnor, 2007). Approximately 30% of all patients that received a NMBA throughout the intraoperative phase show clinical signs of impaired function of the pharyngeal and esophageal muscles which are used as protective mechanisms for the airway (Robertis et al., 2016). It is also alarming that not all patients will show obvert clinical signs of recurarization until respiratory distress and hypoxemia. Farhan et al. (2014) found that PORC increased the risk of respiratory adverse events, postoperative weakness, prolonged recovery, and increased postoperative care unit (PACU) stay. The authors defined a respiratory adverse event as either impaired hypoxic ventilatory drive, impaired respiratory muscle function, impaired protection of airway from aspiration, or critical situation that required supplemental oxygen to maintain saturations greater than 90%. Due to the associated, potentially fatal adverse events, adequate reversal from neuromuscular blockade is a clinically serious problem. Specific patient identifiers

associated with an increased risk of complications related to the use of NMBAs are elderly patients; morbidly obese patients; patients presenting with preexisting neurological, neuromuscular, respiratory, cardiac, renal, and liver disease; and patients with contraindications to currently used reversal agents (Carron, Baratto, Zarantonello, & Ori, 2016). Complications secondary to PORC can be costly for our healthcare organizations, in which the cost of managing postoperative patients with respiratory complications was nearly $63,000 compared to only $5,000 for uncomplicated cases per patient (Farhan et al., 2014).

Another concern related to undesired paralysis is during a rapid sequence induction with rocuronium, a non-depolarizing NMBA, to control the patient's airway with the inability to intubate. This method of anesthesia care is used to protect an airway for patients that are considered high risk for aspiration. This is a common practice for patients that are obese, pregnant, have delayed gastric emptying, have active gastrointestinal reflux, or requiring emergent surgery and have not fasted prior to surgery. The most commonly used NMBA for rapid sequence cases is succinylcholine because of its short duration of action of 5-10 minutes, however there are many situations the contraindicate its use. Contraindications to the use of succinylcholine include pediatric males; history of malignant hyperthermia, atypical pseudocholinesterase, or muscular dystrophies; recent stroke, burn, or musculocutaneous injuries; and chronic renal failure with hyperkalemia (Naguib, 2015). The only other NMBA for these cases is rocuronium, which has a duration of 35 minutes for normal, healthy patients. As a result, to its longer duration of action, there is the warranted concern of a cannot ventilate-cannot intubate (CVCI) event (refer to 'definitions of terms' section for clarity of CVCI event). This can lead to respiratory failure and cardiac arrest without the employment of emergency respiratory

strategies. Current NMBA reversal practices are simply not timely enough for these rare events, however there is a new reversal breakthrough that has been found to be effective and promising.

Current Reversal Practices and CPGs

Currently the universal practice of reversing patients' neuromuscular blockade is with the use of neostigmine. Neostigmine is an acetylcholinesterase inhibitor that does not directly affect the NMBA, but only indirectly increases acetylcholine in the neuromuscular junction to increase competition for nicotinic receptor sites (Naguib, 2015). There are many side effects with the use of acetylcholinesterase inhibitors that necessitates the addition of an anticholinergic drug to offset these symptoms. Common symptoms include bradycardia, bronchospasm, and other muscarinic side effects that are undesirable for surgical patients recovering from anesthesia (Liu, et al., 2017). The addition of an anticholinergic drug, such as glycopyrrolate matched with neostigmine, is associated with its own unwarranted side effects, such as tachycardia and dry mouth (Naguib, 2015). Further, neostigmine is unable to reverse deep neuromuscular blockade, as assessed be a train-of-four (TOF) count less than two, which requires delayed recovery and increased hospital costs (Kopman & Eikermann, 2009) (refer to 'definitions of terms' section for clarity of TOF). It is also alarming that even with a TOF count of four, which is the maximum twitch count, there is the possibility of 70% blockade of nicotinic receptors which still predisposes the patient to PORC (Liu, et al., 2017).

Recent Reversal Breakthrough

The US Food and Drug Administration has recently approved a new reversal agent, sugammadex, which is revolutionizing how practitioners treat neuromuscular blockade in surgical patients. Sugammadex was originally approved in the European Union in 2008 and has

made significant advancement in the management reversing neuromuscular blockade (Keating, 2016). It has been approved in numerous countries around the world, but has only recently been approved in the US. Sugammadex's mechanism is completely different compared to acetylcholinesterase inhibitors, in that it directly affects the NMBAs that were administered intraoperatively. Sugammadex reverses neuromuscular blockade by encapsulating and inactivating aminosteroid NMBAs by creating a 1:1, inactive complex. Further, there is a negative gradient that is formed that causes more aminosteroid NMBAs to diffuse away from the neuromuscular junction (Naguib, 2015). The end result of sugammadex is a reduced amount of free NMBA that is able to block nicotinic receptor sites in the neuromuscular junction, thus causing a reversal of neuromuscular blockade (Keating, 2016). Sugammadex is biologically inactive molecule that has very few side effects and is excreted in the urine unchanged (Naguib, 2015). One limiting factor is that sugammadex only reverses steroidal-induced neuromuscular blockade, as seen with rocuronium and vecuronium; it is unable to reverse cistracurium or atracurium-induced neuromuscular blockade related to its chemical structure (Naguib, 2015). The use of sugammadex has also been attributed to allergic reactions, which is an undesirable reaction of the immune system to a drug or allergen, similarly to how NMBAs have been attributed with allergic reactions. Obviously, it is pertinent that anesthesia personnel are always prepared to treat allergic reactions or anaphylaxis for all perioperative patients. Sugammadex has been attributed to a full reversal from neuromuscular blockade in only three minutes after administration, which is far lower than neostigmine's 10 to 30-minute onset of action (Chambers et al., 2010; Lexicomp, 2017; Keating, 2016). This makes the addition of sugammadex into anesthesia practice highly advantagous for prevention of potential CVCI catastrophic outcomes.

The speed of reversal associated with sugammadex has the capability of drastically reducing the risk of morbidity and mortality in a CVCI events after rocuronium induced neuromuscular blockade (Chambers et al, 2010).

Definitions of Terms

Postoperative Residual Recurarization (PORC)

PORC is the persistent residual paralysis after the administration of a NMBA following recovery of anesthesia (Farhan et al., 2014). PORC is clinically defined as a TOF ratio of less than 0.9 (Carron, Zarantonello, Tellaroli, & Ori, 2016).

Train-of-Four Monitoring (TOF)

TOF monitoring is typically used to assess the depth of neuromuscular transmission when NMBA are administered to block musculoskeletal activity. The TOF ratio is the comparison of the fourth twitch to the first twitch to evaluate the degree of weakness, and is able to estimate the percentage of neuromuscular blockade from 70 to 100% (Nagelhout, 2016). It has been well established that recovery from neuromuscular blockade can be monitored with a TOF ratio greater than 0.9 (Robertis, et al., 2016). Acceleromyography provides objective monitoring of the TOF ration and is considered the gold standard, however it is rarely employed (Carron et al., 2016).

Rapid Sequence Induction

Rapid sequence inductions are employed when patients are considered to be at risk for aspiration of gastrointestinal contents, which is associated with various sequela. It involves rapid intravenous administration of an anesthetic and paralytic without bag mask ventilation prior to direct laryngoscopy and tracheal intubation. This technique prevents insufflation of the stomach

and minimizes intra-abdominal pressure fluctuations that leads to vomiting and aspiration. Patients at risk for aspiration include active comorbidities of obesity, pregnancy, gastrointestinal reflux, bowel obstruction, and other causes of full stomach. Rapid sequence inductions are associated with a wide range of potentially dangerous adverse events and death (Carron et al., 2016). Currently the only NMBAs with a rapid enough onset of action are succinylcholine and rocuronium. In patient scenarios that prevent the use of succinylcholine, it is recommended to have sugammadex available to potentially reverse the longer duration of rocuronium (Chambers et al., 2010).

Cannot Ventilate – Cannot Intubate (CVCI)

CVCI events are related to the provider's inability to either intubate the trachea or ventilate with bag-mask ventilation (Carron et al., 2016). When longer duration NMBAs are used for muscle relaxation the patient is unable to resume spontaneous ventilation or maintain a patent airway, and the risks of complications are highly increased.

Local Problem

This DNP project was designed for the development of a CPG for a healthcare organization that has been resistant to the incorporation of sugammadex into the practice setting. The designated facility currently does not employ the use of sugammadex for fear of increased costs and perception that it is not clinically needed. The institution is currently considering the addition of sugammadex to the pharmacy's formulary but does not have a current protocol or guideline for appropriate reversal measures. The development of a facility focused CPG would include evidence-based recommendations on appropriate clinical scenarios and patient populations in which sugammadex would be a highly appropriate measure.

Associated Comorbidities

As noted previously, there are many comorbidities that have been associated with PORC and increased postoperative complications, such as obesity, obstructive sleep apnea, and chronic respiratory diseases. Obesity has been a highly prevalent issue in the US affecting 37% of the adult population and 17% of the pediatric population (Ogden, Carroll, Fryar, & Flegal, 2015). Obstructive sleep apnea has been diagnosed for more than 18 million people in the US; as well there is a high correlation with obesity, in which the estimated rate of undiagnosed sleep apnea is 80 to 95% of obese, perioperative patients (Nagelhout, 2014). The CDC found that 12.8 million or 5.2% of US adults have been diagnosed with chronic obstructive pulmonary disease (2015). Other patient conditions that could place a patient at an increased risk comprise cardiovascular, neuromuscular, kidney, and liver disease (Carron et al., 2016). Lastly, it has been established that geriatrics are also at an increased risk to PORC due to a decreased effectiveness in eliminating NMBAs and decreased respiratory compliance. The geriatric population remains highly prevalent at the designated facility in the Phoenix-Metropolitan area. In the State of Aging and Health in America 2013, the CDC predicts that by 2030 the geriatric population will account for nearly 72 million or 20% of the total US population. This is only complicated by the fact that nearly two out of every three geriatric patients have multiple comorbidities (CDC, 2013).

Current Guidelines

The significance of PORC in regards to patient safety and postoperative outcomes has been noted by several global specialty organizations worldwide. However, unlike our European counterparts, the American Society of Anesthesiologists (ASA) does not mandate the best-practice of peripheral nerve monitoring for patients that received muscle relaxation (Brull &

Kopman, 2017). Furthermore, the current nationally accepted CPG for postanesthetic care does not include the use of sugammadex for reversal of blockade. The 2013 updated report by the ASA on *Practice Guidelines for Postanesthetic Care* states that "specific antagonists should be administered for reversal of residual neuromuscular blockade when indicated," but only includes two approved acetylcholinesterase inhibitors, neostigmine and edrophonium (Apfelbaum et al., 2013). Apfelbaum et al. (2013) identified the major premise of the CPG to evaluate current evidence-based recommendations for assessment, monitoring, and management with the goal to enhance patient safety for perioperative patients. The logical reasoning for sugammadex's absence in the nationally recognized CPG is the date of revision, in that it was only recently approved in the US late 2015. In response to currently published literature, sugammadex's inclusion into the ASA CPG as an appropriate reversal agent for patients recovering from rocuronium and vecuronium-induced neuromuscular blockade is imperative. Due to the non-current, nationally published guidelines on postanesthetic care, there is an identified gap in current EBP and need for promotion of best-practices at the organizational level.

Specific Institutional Focus

This DNP project will take place in a specified healthcare organization in the Phoenix-Metropolitan area. The main barrier to the implementation of sugammadex into the practice protocol is the perceived increase per patient cost of reversal. Current cost of reversal for an average 70-kilogram patient is $61 for 5 milligrams of neostigmine mixed with $36 for 1 milligram of glycopyrrolate, for a total cost of $97 (Lexicomp, 2017). In comparison the current costs of sugammadex is $114 per patient, which is around $17 more than the neostigmine-glycopyrrolate combination (Lexicomp, 2017). As the price differences vary from facility to

facility, it is estimated that there is an increased cost of $8 to $51 per reversal per patient (Lexicomp, 2018). However, this does not take into account the potential reduced perioperative stay costs and poor outcome treatment costs. Complications secondary to residual paralysis can significantly impact organizational budgets, in which the cost of managing postoperative patients with respiratory complications due to PORC was nearly $63,000 compared to only $5,000 for uncomplicated cases (Farhan et al., 2014). The overall reversal cost after all factors are considered does not produce a clear result, leading to the presumption that it could be highly beneficial to incorporate the use of sugammadex for high-risk patients. It is the healthcare organization's responsibility to adapt current practices to the current, evidenced-based recommendations. Many of the anesthesia providers at the designated facility have vocalized their concerns to placing greater significance to minute increases in healthcare costs rather than evidence-based recommendations.

Significance to Advanced Practice Nursing

Data implies that PORC is a common concern for all perioperative patients that receive NMBAs, and demographic trends in the US are placing more and more patients at risk for poor postoperative outcomes. As DNPs are becoming mainstream in providing effective anesthesia care, it becomes essential that evidence-based recommendations are applied to clinical practice thus enhancing patient safety. It is the role of a DNP to continue propelling change forward for the betterment of our patient populations, and to integrate the best available research with clinical expertise through EBP (DiCenso, Guyatt, & Ciliska, 2005). CPGs are an integral component of EBP, in that they provide clear guidelines through evidence-based recommendations to promote patient care and the rate of successful patient management

(Zaccagnini & White, 2011). The role of DNPs also includes overcoming barriers of the status quo that might stand in the way of implementing best practices.

The primary barrier to the full acceptance of sugammadex is the perceived increased cost, in that sugammadex is monetarily more expensive per vial. It is concerning that many healthcare organizations balance perceived profits with EBP, in which the perceived costs should be a nominal factor attributed to providing best practice to patients. A CPG for the regulated use of sugammadex could minimize this barrier for the many reluctant healthcare organizations and ensure that reversal agents are available for high risk patients and in emergent scenarios. Sugammadex should at minimum be made available in every healthcare organization for the occurrence of an NMBA overdose, similarly to naloxone being available for opioid overdose or flumazenil being available for benzodiazepine overdose. The unwillingness to implement the use of sugammadex, even if regulated, is a relative disregard and ignorance to EBP and places perioperative patients at risk.

Purpose

The purpose of this DNP project was to identify the current evidence-based recommendations from current literature for the reversal of neuromuscular blockade and develop a CPG at the organizational level with the input from anesthesia specialized consultants. The overall aim was to develop a high quality CPG ready for application in the clinical environment. The focus was on a facility without a CPG and was resistant to the full, unregulated use of sugammadex.

Study Question

The project question for this DNP project is: Did the development of a CPG regarding the use of sugammadex produce quality-driven, evidence-based recommendations using efficient and transparent methodology with interdisciplinary applicability?

FRAMEWORK AND SYNTHESIS OF EVIDENCE

Theoretical Framework

The overarching theory that guided this DNP project is Lewin's Change Theory (LCT). The theory is considered one of the architypes to change theories, and has been utilized in numerous innovative changes (Kaminski, 2011). Changes in the clinical setting, such as the implementation of evidence-based recommendations in a CPG, are often pressured and chaotic which often leads to a lack of engagement from the operational stakeholders. This DNP project also utilized the Knowledge to Action (KTA) framework to implement the change in an effective manner. The inherent focus of the framework is to integrate research into practitioner's practice as an instrument to enhance patient outcomes. The incorporation of theoretical frameworks allows a systematic and structured process for innovative change that reduces the risk of failure. The development of a CPG is a critical component to EBP in that it provides protocol driven recommendations, enhances treatment efficiency, and minimizes differences between practitioners (Tymkow, 2011). The incorporation of the LCT and KTA framework was ideal for this process as it describes the systematic approach to applying an innovative change agent into clinical practice.

Lewin's Change Theory

Developed in 1951 by Kurt Lewin, LCT recognizes that a change agent must navigate through three distinct phases prior to becoming a part of a healthcare organization (Mitchell, 2013). The three phases that a change agent must traverse are the unfreezing phase, changing phase, and refreezing phase (Kaminski, 2011). However, the change agent must not only navigate through the three phases, but it must overcome resistance and barriers to change. LCT developed the key concept of force field analysis, which describes that all human behaviors are depended upon precarious forces that are either pushing us forwards or pulling us back from certain behaviors (Mitchell, 2013). There are three aspects to the force field analysis, which are the driving forces, the restraining forces, and equilibrium (Kaminski, 2011). Driving forces are those that guide use towards a change, which is opposed to restraining forces that propel us away (Kaminski, 2011). Equilibrium is reached at the point that the driving forces are equal to the restraining forces, and can be considered the status quo in many clinical scenarios (Kaminski, 2011). The three phases of LCT provides a simple illustration of clinical change, assists with innovative change, and correlates specifically to the development of a CPG for the regulated use of sugammadex (Figure 1).

FIGURE 1. Adaptation of Lewin's change theory.

Unfreezing is the first phase of this theory, in which entails the examination of the status quo and current practices with identification of a need to change. The use of sugammadex in the perioperative phase for reversal of neuromuscular blockade has been a new concept for many practitioners, and is just starting to get traction. The recent literature support for sugammadex is a knowledge focused trigger that alerts practitioners to the ineffective, current practices. Knowledge focuses triggers include new published guidelines or research that recommends a change to how care is provided to enhance patient outcomes (Titler, 2010). It remains critical in the unfreezing phase to identify the driving forces in the early stages to push the change forward (Sutherland, 2013). Driving forces in this project include literature support of sugammadex's simplicity of use and significantly improved patient outcomes. Restraining forces could include the hesitancy to changing the way it has always been done and inadequate knowledge to the efficiency of reversal with sugammadex. Enhancing the driving forces while diminishing the

restraining forces, such as with dialogue and education, will encourage the staff to let go of outdated practices (Kaminski, 2011).

The change phase centers around the implementation of change into the clinical phase. This DNP project focused on the development of a CPG on the regulated use of sugammadex, from current evidence-based recommendations. The current, relevant evidence for sugammadex was assembled, analyzed, and synthesized, with verification that sufficient evidence is available. It would be beneficial during this phase to include a development timeline (Sutherland, 2013). The end goal of the change phase was to set a new equilibrium and move away from the status quo, which will need continually uplifting of driving forces. The CPG development included receiving input from an anesthesia consultant for a clinical expertise component. The primary restraining force to the incorporation of sugammadex into the perioperative phase is the fear of increased reversal costs per patient. This was minimized with the CPG's focus on regulated use for high risk patients, instead of the notion that sugammadex needs to be used on every patient, every time.

The establishment of the new guideline as a permanent practice in the perioperative phase would be evident in the last phase of refreezing (Kaminski, 2011). It was necessary to evaluate the CPG's effectiveness and simplicity of use to ensure sustainability. To overcome the restraining force of knowledge and training deficit of the ancillary staff, it was appropriate ensure ease of use and applicability of the CPG. It is the responsibility of DNP prepared APRNs to take action in their own practice, make changes, and engage other practitioners to improve care (Mitchell, 2013). The use of LCT provided the overarching theoretical approach to change, by unfreezing the status quo of ineffective neuromuscular blockade reversal, implementing the

use of sugammadex through a CPG development, and sustaining change through application of high quality, literature supported guidelines.

Knowledge to Action (KTA) Framework

The KTA framework was designed to translate current evidence into current practice in an effective manner. Graham et al. (2006) highlighted that nearly 45% of patients are not receiving care according to current literature, and nearly 25% of patients are receiving interventions that are either ineffective or potentially harmful. APRNs need to be continually assessing current literature and enhancing their knowledge base with the intent to treat patients in an evidence-based approach, as opposed to solely working from previous clinical experience and perceived expertise (Doody & Doody, 2011). The KTA framework entails a step by step approach to implementing current evidence into a clinical setting to improve patient outcomes. This DNP project's focus was to implement current evidence-recommendations on the use of sugammadex into anesthesia practice, and used the KTA framework as a systematic guide. The authors developed a knowledge to action process that incorporates knowledge creation and an action cycle for implementation (Graham et al., 2006).

Knowledge creation is described as moving through a funnel, in that it becomes more refined and valuable for stakeholders as one delves through the research (Figure 2). The funnel begins with a knowledge inquiry that entails sifting through unmanageable amount of evidence, then moves into the synthesis of relevant and current literature (Graham et al., 2006). Knowledge synthesis describes the literature review of relevant and current evidence to the inquiry, and ensures that the evidence supports that actual change. It is strongly encouraged to incorporate systematic reviews and meta-analysis into this phase of knowledge creation (Graham et al.,

2006). The final component of knowledge creation is the development of knowledge tools and products, such as seen with CPGs the provide clearly established recommendations (Graham et al., 2006). The overall goal in the first stage of the KTA framework for this DNP project was the development of a CPG on the regulated use of sugammadex.

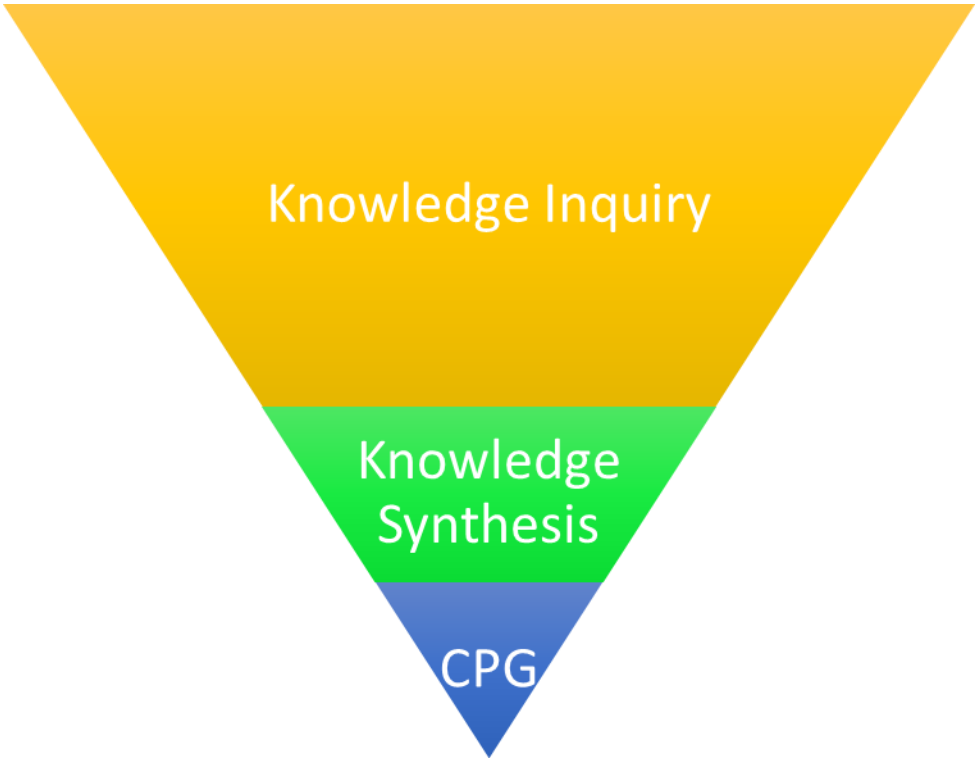


FIGURE 2. Adaptation of KTA knowledge creation.

After the knowledge creation was completed with the development of a CPG, it underwent the action cycle of implementation to a clinical setting that applies an effective step by step approach (Figure 3). The initial steps in the action cycle includes the identification, selection, and adaption of knowledge at the organizational level (Graham et al., 2006). The designated facility was evaluated on its current practices and need for the regulated use of sugammadex. Assessing barriers to change was the next step to the action cycle (Graham et al., 2006). There are numerous healthcare organizations that currently do not use sugammadex due

to the fear of increased costs per patient and change to ‘how it has always been done,’ however this is a great time to increase awareness of the issue and enhance driving forces. The next step included the tailoring of the CPG for applicability at the organizational, which was enhanced through inclusion of organizational insights from current anesthesia providers and key stakeholders (Graham et al., 2006). Further, this step included the adaption of the CPG with expert opinions. The last steps of the action cycle included evaluation of the quality of the CPG and methods to sustain the change (Graham et al., 2006). Evaluation of the CPG was provided via an CPG assessment tool. The sustained use of knowledge was encouraged with the CPG being made available to the healthcare organization and dissemination of results to its quality.

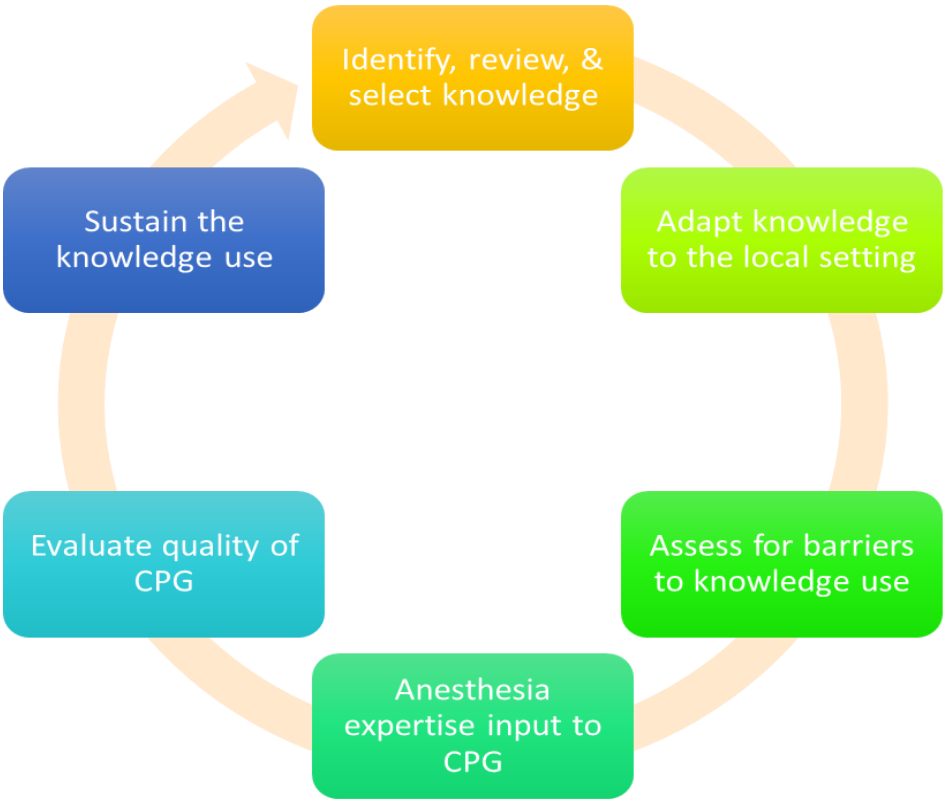


FIGURE 3. Adaptation of KTA action cycle.

Synthesis of Evidence

Search Strategy of Literature Review

The literature review was conducted using highly credible electronic databases, including PubMED, CINAHL, and Cochrane Library. The search criteria focused on current recommendations and evidence pertaining to the use of sugammadex published since 2010 with full text availability. Evidence was appraised by its' hierarchy of evidence, in that systematic reviews and meta-analyses were included as the highest quality studies followed by random controlled trials. Key search terms were included, but not limited to, sugammadex, neostigmine, neuromuscular blockade, obesity, geriatrics, liver disease, renal disease, sleep apnea, rapid sequence induction, safety, efficacy, and pediatrics. The search focus was specific to the DNP project and related to the use of sugammadex for the reversal of neuromuscular blockaded in the perioperative environment (Table 1).

TABLE 1. *Synthesis of the effectiveness of sugammadex for reversal of neuromuscular blockade.*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
Abdulatif, Lotfy, Mousa, Afifi, & Yassen (2018) Sugammadex antagonism of rocuronium-induced neuromuscular blockade in patients with liver cirrhosis undergoing liver resection: a randomized controlled study.	Compare the recovery time of sugammadex and neostigmine in reversal of rocuronium induced NMB in patients with liver cirrhosis and controls undergoing liver resection.	Randomized control trial.	27 patients with Child-Pugh class "A" liver cirrhosis and 28 patients with normal liver function, all from ages 18 to 60 years undergoing liver resections (N= 55). Group 1(n= 14): Patients with normal liver function that received sugammadex. Group 2 (n= 14): Patients with normal liver function that received neostigmine. Group 3 (n= 13): Patients with liver cirrhosis that received sugammadex. Group 4 (n= 14): Patients with liver cirrhosis that received neostigmine. Ethical approval and patient consent.	Data collection performed using SPSS for Windows. Numerical values summarized as means. - ANOVA - Post-hoc Tuckey test - Chi-square test - Fisher's Exact test Compare the reversal of rocuronium induced NMB with sugammadex and neostigmine. Primary outcome: - Time from antagonist administration to a TOFR > 0.9. Secondary outcomes: - Durations of intubating and top up doses of rocuronium. - Length of stay in the PACU. - Incidence of postoperative recurarization.	There was a faster recovery time for patients with sugammadex reversal for patients with liver disease (3.1 min) and normal liver function (2.6 min) compared to patients reversed with neostigmine with liver disease (14.5 min) and normal liver function (15.7 min; $p<0.001$). There was a shorter stay in PACU for patients reversed with sugammadex for patients with liver disease (23 min) and normal liver function (22.8 min) compared to patients reversed with neostigmine with liver disease (43.9 min) and normal liver function (43.2 min; $p<0.001$). Conclusion: sugammadex rapidly reverses rocuronium induced NMB in patients with Child-Pugh class "A" liver cirrhosis undergoing liver resection.
Carron, Zarantonello, Lazzarotto, Tellaroli, & Ori (2017) Role of sugammadex in accelerating postoperative discharge: A meta-analysis.	To review and evaluate the evidence comparing sugammadex and neostigmine related to patient discharge after general anesthesia.	Systematic review and meta-analysis. Study design using PRISMA methodology.	Six randomized controlled trials. Patients totaling 518. Setting in a university medical hospital.	Comprehensive literature search conducted using PubMed, Web of Science, Google Scholar, and Cochrane Library electronic databases. Measurement of time to discharge after a NMB reversal with sugammadex compared to neostigmine.	Discharge from the OR to PACU was significantly faster with sugammadex (MD= 22.14 min; 95% CI; $P < 0.00001$). Discharge from the OR to PACU with deep NMB had even greater recovery with sugammadex (MD= 30.05 min; 95% CI; $P < 0.002$). Discharge from the PACU to surgical ward was significantly

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
				- Discharge from the OR to the PACU. - Discharge from the OR to the PACU with deep NMB. - Discharge from the PACU to surgical ward. - Discharge of morbidly obese patients from the PACU to surgical ward.	faster with sugammadex (MD= 16.95 min; 95% CI; P= 0.0469). Discharge of morbidly obese patients from the PACU to surgical ward was significantly increased with the use of sugammadex (MD= 8.75 min; 95% CI; P < 0.0001). Conclusion: sugammadex accelerates postoperative discharge of patients after general anesthesia compared to neostigmine.
Carron, Zarantonello, Tellaroli, & Ori (2016) Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials.	To review and evaluate the evidence related to the effectiveness and safety of sugammadex compared to neostigmine for reversing NMB in adults.	Meta-analysis. Study design using PRISMA methodology.	Thirteen randomized controlled trials. Patients totaling 1384. Setting in a university medical hospital.	Comprehensive literature search conducted using PubMed, Web of Science, and Cochrane Library for electronic databases. Only included English-language articles. Measurement of sugammadex compared to neostigmine on reversing NMB. Primary outcomes: - Speed of reversal. - TOFR after reversal of NMB. Secondary outcomes: - Risk of postoperative residual recurarization after extubation. - Risk of global adverse events. - Postoperative nausea and vomiting. - Reported pain.	Speed of recovery was significantly faster with sugammadex (MD= -1.79 min; 95% CI, P < 0.0001). TOFR was assessed significantly higher with the use of sugammadex after reversal (MD= 0.18; 95% CI; P < 0.0001). Sugammadex was found to have a significantly lower risk of postoperative residual recurarization (OR= 0.05; 95% CI; P = 0.0068), global adverse events (OR= 0.47; 95% CI; P < 0.0001), respiratory adverse events (OR= 0.36; 95% CI; P = 0.0386), cardiovascular adverse events (OR= 0.23; 95% CI; P = 0.0036), and postoperative weakness (OR= 0.45; 95% CI; P = 0.0409). No significant differences between sugammadex and neostigmine on postoperative nausea and vomiting, pain, neurological adverse events, and change in laboratory test values.

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
				- Risk of neurological adverse events. - Changes in laboratory test values.	Conclusion: sugammadex is superior to neostigmine due to its speedier recovery and lower risk of adverse events.
Chambers, Paulden, Paton, Heirs, Duffy, Hunter, Sculpher, & Woolacott (2010) Sugammadex for reversal of neuromuscular block after rapid sequence intubation: a systematic review and economic assessment.	Review and evaluate the evidence on the efficacy and cost-effectiveness for the use of sugammadex for reversal of NMB after RSI.	Systematic review.	Three random- controlled trials. Patients totaling 336 adults.	Comprehensive literature search conducted using MEDLINE, CINAHL, Science Citation Index, BIOSIS, EMBASE, and CENTRAL for electronic databases. Two placebo controlled trials to compare the use of sugammadex to reverse RSI dose of rocuronium to that of a placebo (spontaneous recovery). One controlled-trial to compare the RSI of rocuronium/ sugammadex to succinylcholine with spontaneous recovery. - Time to recovery assessed by T1/T10=0.1 - Time from start of NMBA to TOFR > 0.9 - Time of sugammadex administration to TOFR > 0.9	Sugammadex was found to significantly reduce the time of reversal from a RSI dose of rocuronium from 90-120 min. Patients that received rocuronium/sugammadex RSI compared to succinylcholine had significantly time of T1/T10 (4.4 min to 7.1 min) and to TOFR > 0.9 (6.2 min vs. 10.9 min). Time from sugammadex administration to TOFR > 0.9 was 2.2 min ($P < 0.00001$). Limited economic assessment due to lack of suitable evidence. Conclusion: the use of sugammadex for the reversal of rapid sequence induction dose of rocuronium is effective.

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
Evron, Abelansky, Ezri, & Izakson (2017) Respiratory events with sugammadex vs. neostigmine following laparoscopic sleeve gastrectomy: a prospective pilot study assessing neuromuscular reversal strategies.	Determine if the use of sugammadex compared to neostigmine would result in lower respiratory events for obese patients undergoing sleeve gastrectomy surgeries.	Randomized control trial.	N= 57 obese patients undergoing laparoscopic sleeve gastrectomy. Inclusion criteria included ASA classification I-III, > 18 years of age, without neuromuscular, renal, or liver disease. Group 1 (n= 32): Patients received reversal from NMB with 2 mg/kg of sugammadex. Group 2 (n= 25): Patients received reversal from NMB with neostigmine 2.5 mg. Single site study in Hollon, Israel. Ethical approval through IRB and patient consent.	Data collection performed using SPSS for Windows. Numerical values summarized as means. - Kolmogorov-Smirnov test - chi-square test - t test - Fisher exact test Measurement of groups were compared related to the reversal of sugammadex to neostigmine for rocuronium-induced NMB. - Oxyhemoglobin saturation in the PACU. - TOF counts prior to administration of reversal agent. - Unexpected ICU admissions. - Incidences of reintubation.	Oxyhemoglobin saturation was significantly higher in the PACU with the use of sugammadex compared to the neostigmine group (96.72 vs. 95.80; $p < 0.01$). Minimal oxyhemoglobin saturation was lower in the neostigmine group at 93% compared to 94% in the sugammadex group ($p= 0.01$). TOF count was significantly lower in the sugammadex group prior to administration of the reversal agent compared to the neostigmine group (2.53 vs 3.48; $p < 0.01$). Conclusion: The use of sugammadex for reversal of NMB compared to neostigmine was associated with higher oxyhemoglobin saturation, despite lower TOF count prior to reversal.
Hristovska, Duch, Allingstrup, & Afshari (2017) The comparative efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade in adults. A Cochrane systematic review with meta-analysis and trial sequential analysis.	Review and evaluate the evidence for effectiveness of sugammadex in reversal of NMB compared to neostigmine for adult patients undergoing general anesthesia.	Systematic review and meta-analysis. Study design using PRISMA methodology.	41 randomized controlled trials. Patients totaling 4,206 patients.	Comprehensive literature search conducted using CENTRAL, MEDLINE, and Embase for electronic databases. Compared the efficacy of sugammadex and neostigmine.	Time of reversal of NMB was significantly faster with sugammadex from 2nd twitch to TFOR > 0.9 (2.0 min vs. 12.9 min; MD 10.2; 95% CI). Time of reversal of NMB was significantly faster with sugammadex from post-tetanic count 1-5 to TOFR > 0.9 (2.9

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
				Primary outcomes: - Recovery time from 2nd twitch to TOFR > 0.9. - Recovery time from post-tetanic count1-5 to TOFR > 0.9. Secondary outcomes: - Risk of drug-induced adverse events. - Risk of serious adverse events.	min vs. 48.8 min; MD 45.8; 95% CI). Sugammadex had significantly less drug-induced adverse events (RR 0.60; 95% CI). Specifically, less bradycardia (RR 0.16; 95% CI), PONV (RR 0.52; 95% CI), and residual paralysis (RR 0.40; 95% CI). There was no significant difference in serious adverse events. Conclusion: sugammadex reverses NMB more rapidly than neostigmine and is associated with fewer adverse events.
Liu, Wang, Yan, Fan, Xue, & Wang (2017) The efficacy and safety of sugammadex for reversing postoperative residual neuromuscular blockade in pediatric patients: A systematic review.	Review and evaluate the evidence on the efficacy and safety of sugammadex for reversing NMB in pediatric patients.	Systematic review, and meta-analysis. Study design using PRISMA methodology.	Ten randomized controlled trials. Patients totaling 580 pediatric patients. Setting in a medical hospital in Beijing, China.	Comprehensive literature search conducted using MEDLINE, PubMed, Web of Science, EMBASE, and CENTRAL for electronic databases. Primary outcome: - Time interval from administration of reversal agent to TOFR > 0.9. Secondary outcome: - Incidences of any drug-related adverse events.	There was a significantly reduced time to TOFR > 0.9 for pediatric patients that received sugammadex compared to neostigmine (WMD= -8.51 min; 95% CI). There was a significantly reduced risk of drug-induced bradycardia with the use of sugammadex compared to neostigmine (RR= 0.08; 95% CI). There was not a significant change related to nausea and vomiting, diarrhea, and bronchospasm.

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
					Conclusion: compared to neostigmine or a placebo, sugammadex reverses rocuronium-induced NMB in pediatric patients rapidly and safely.
McDonagh, Benedict, Kovac, Drover, Brister, Morte, & Monk (2011) Efficacy, safety, and pharmacokinetics of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in elderly patients.	Compare the efficacy, safety, and pharmacokinetics of sugammadex administration for reversal of moderate NMB in adults vs. elderly patients.	Prospective, randomized control trial.	N= 150 adult patients undergoing general anesthesia requiring NMB, with ASA classification I-III. Group 1 (n= 48): Adult patients aged 18-64 years old. Group 2 (n= 62): Elderly patients aged 65-74 years old. Group 3 (n= 40): Old-elderly patients aged > 74 years old. Multicenter, 14 surgical centers in the United States. Ethical approval and patient consent.	Data collection performed using SPSS for Windows. - two-way ANOVA model Measurement of groups were compared related to the reversal of rocuronium induced NMB with sugammadex 2 mg/kg. - Time from the administration of reversal to TOFR > 0.9.	Time from administration of sugammadex to a TOFR > 0.9 was increased the most in old-elderly/elderly groups (2.7-3.2 min) than the adult group (2.0-2.6 min; P= 0.022). Recovery was estimated to be 0.7 min faster in adults compared to patients 65 years and older. Sugammadex was tolerated by all patients, no adverse events were noted. Conclusion: sugammadex reverses rocuronium-induced NMB rapidly and safely in adults of all ages.

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
Robertis, Marinosci, Romano, Piazza, Iannuzzi, Cirillo, Simone, & Servillo (2016) The use of sugammadex for bariatric surgery: analysis of recovery time from neuromuscular blockade and possible economic impact.	Compare recovery times after the administration of sugammadex and neostigmine, and assess the possible economic impact.	Retrospective, non-randomized study.	N= 95 morbidly obese patients (body mass index > 40 kg/m2) undergoing bariatric surgery. Group 1 (n= 50): Obese patients that received rocuronium and sugammadex for NMB and reversal. Group 2 (n= 49): Obese patients that received either rocuronium or cisatracurium and neostigmine for NMB and reversal. Single surgical center in Naples, Italy. Local ethics approval by the University of Naples Federico II approved.	Data collection performed using SPSS for Windows. - Wilcoxon rank sum test - Mann-Whitney U test Measurements were made to compare the reversal of sugammadex to neostigmine in recovery of NMB. - Mean recovery time from reversal to a TOFR > 0.9. - Mean theater occupancy (time from the start of anesthesia time until the time the patient was transported to the PACU). - Mean time to obtain an Aldrete score of 10 (indication that the patient is ready to be discharged from the PACU).	The mean recovery time was significantly faster in the sugammadex group than the neostigmine group (1.4 min vs. 26.4 min, $P < 0.05$). All patients that received sugammadex had received a TOFR > 0.9 within 5 minutes. The mean theater occupancy time was significantly faster in the sugammadex group than the neostigmine group (93.3 min vs. 116.6 min, $P < 0.05$). The mean time to achieve an Aldrete score of 10 was significantly faster in the sugammadex group than the neostigmine group (16 min vs. 21.8 min, $P < 0.05$). Conclusion: reversal from NMB is significantly faster in obese patients with sugammadex compared to neostigmine.
Souza, Tardelli, Tedesco, Garcia, Caparros, Alvarez-Gomez, & Oliveira (2015) Efficacy and safety of sugammadex in the reversal of deep neuromuscular blockade induced by rocuronium in patients with end-stage renal disease:	Compare the efficacy and safety of sugammadex administration for reversal of profound NMB in patients with renal failure and normal renal function.	Prospective, randomized control trial.	N= 40 patients undergoing kidney transplantation. Group 1 (n= 20): Patients with renal failure as defined as a creatinine clearance < 30. Group 2 (n= 20):	Data collection performed using SPSS for Windows. - Kolmogorov-Smirnov test - Chi-square test - t test - Fisher exact test - Mann-Whitney test	The mean time for reversal of NMB from sugammadex was prolonged in the patients with renal failure (5.6 min) compared to the normal renal function group (2.7 min; P= 0.003).

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
A comparative prospective clinical trial.			Patients with with normal renal function as defined as a creatinine clearance > 90. Two university hospitals in Sao Paulo, Brazil. Ethical approval and patient consent.	Measurement of groups were compared related to the reversal of rocuronium induced NMB with sugammadex. - Time from rocuronium to NMB. - Time from the administration of reversal to TOFR > 0.9. - Adverse events related to NMB.	No adverse events or evidence of recurarization of NMB were observed. Conclusion: Sugammadex effectively and safely reverses profound rocuronium induced NMB in patients with renal disease, however recovery is slightly prolonged.
Unal, Baran, Mutlu, Ural, Akkaya, & Ozlu (2015) Comparison of Sugammadex versus Neostigmine Costs and Respiratory Complications in Patients with Obstructive Sleep Apnoea.	Compare the efficacy of sugammadex and neostigmine in reversing rocuronium induced NMB.	Randomized, control trial.	N= 74 patients with ASA classification of I or II, with a diagnosed history of obstructive sleep apnea. Group S (n= 37): Patients received reversal from NMB with 2 mg/kg of sugammadex. Group N (n= 37): Patients received reversal from NMB with neostigmine 0.04 mg/kg. Research hospital in Kayseri, Turkey. Ethical approval and patient consent.	Data collection performed using SPSS for Windows. Numerical values summarized as means. - Shapiro-Wilk test - Levine's test - Mann-Whitney U test - chi-square test Measurement of groups were compared related to the reversal of sugammadex to neostigmine for rocuronium-induced NMB. - TOFR after reversal. - OR time. - PACU stay. - Postoperative respiratory complications.	There was a significant faster time to reach TOFR of 0.9 in group S (2 min vs. 8 min, $p < 0.0001$). There was a significant reduction in OR (72.4 min vs. 96.6 min, $p < 0.001$) and PACU times (22.9 min vs. 36.3 min, $p < 0.001$). There was a significant increase in respiratory complications in Group N, including desaturation (12 vs. 3, $P = 0.048$), airway manipulation (12 vs. 3, $P = 0.021$), Re-intubation (3 vs. 0, $P = 0.021$), and use of CPAP device (12 vs. 3, $P = 0.028$). The cost of reversal was greater in Group S (6147.88 TL vs. 3569.5 TL), however the cost

TABLE 1 – *Continued*

Reference	Purpose	Study Design	Sample/ Population	Data Collection / Outcome Measures	Findings/ Conclusion
				- Costs related to NMB reversal, anesthesia care, and treatment.	of complication treatment was less (199.5 TL vs. 3944.6 TL). The total cost was less in Group S compared to Group N (6347.38 TL vs. 7514.15 TL). Conclusion: sugammadex decreases the incidences of postoperative respiratory complications and related costs in patients with obstructive sleep apnea.

PRISMA= Preferred Reporting Items for Systematic Reviews and Meat-Analyses; NMB= Neuromuscular Blockade; OR = Operating room; PACU= Postoperative Care Unit; MD= Mean difference; CI= Confidence Interval; TOFR= Train-of-four ratio; OD= Odds ratio; WMD= Weighted mean difference; RR= Risk ratio; SPSS= Statistical Package for the Social Sciences; ASA= American Society of Anesthesiologists; CPAP= Continuous positive airway pressure; TR= Turkisch Lira; RIS= Rapid Sequence Induction; MD= Mean difference; PONV= postoperative nausea and vomiting.

Sugammadex Reversal in the Perioperative Environment

Sugammadex has been studied extensively related to the reversal of neuromuscular blockade compared to current reversal practices, and has shown unprecedented effectiveness. A recent meta-analysis was completed assessing surgical times comparing sugammadex and neostigmine, and found that sugammadex speed up discharge in adult surgical patients from the operating room (OR) to the postoperative care unit (PACU) by 22 minutes for normal neuromuscular blockade and 30 minutes for deep neuromuscular blockade (Carron, Zarantonello, Lazzarotto, Tellaroli, & Ori, 2017). Another recent meta-analysis compared the effectiveness of sugammadex to neostigmine, and found that it accelerated time to a train-of-four ratio (TOFR) of greater than 90% by nearly 9 minutes in pediatric surgical patients (Liu et al., 2017). Robertis et al. (2016) found that sugammadex increased recovery from neuromuscular blockade 25 minutes quicker than neostigmine in morbidly obese patients, and reduced the OR time by 23 minutes. Another recent meta-analysis compared the effectiveness of sugammadex compared to neostigmine in adult surgical patients, inclusion of 41 separate randomized controlled trials and over 4,200 patients, and found that reversal time was increased by 11 minutes from the second twitch to a TOFR greater than 90%, and was surprisingly increased by 46 minutes from a post-tetanic count of 1-5 to a TOFR greater than 90% (Hristovska, Duch, Allingstrup, & Afshari, 2017). There is substantial amount of evidence that supports that sugammadex is significantly more superior compared to current reversal practices, which is this literature review's predominant strength.

Another strength to this literature review is the evidence that supports sugammadex significantly lowers the risk of perioperative adverse events related to drug-induced reactions and

recurarization, as specified in three different systematic reviews (Carron et al., 2017; Hristovska et al., 2017; Liu et al., 2017). Carron et al. (2017) assessed for adverse events related to PORC and found that sugammadex lowered the risk of global adverse events, respiratory adverse events, cardiovascular adverse events, and postoperative weakness. Some of the respiratory adverse events that were monitored and reduced in these studies included hypoxemia, pulmonary edema, reintubation, upper airway obstruction, and respiratory failure (Carron et al., 2017). Unal et al. (2015) found that the use of sugammadex reduced the risk of postoperative desaturation, airway manipulation, reintubation, and continuous positive airway pressure requirement in patients with obstructive sleep apnea. One study found that sugammadex significantly increased the oxyhemoglobin saturation of obese surgical patients in the postoperative stage despite a lower TOFR prior to reversal (Evron, Abelansky, Ezri, & Izakson, 2017). Some of the cardiovascular adverse events that were reduced with the use of sugammadex included bradycardia, cardiac arrhythmias, and variable atrial pressures (Carron et al., 2017). Three separate meta-analyses found that the use of sugammadex significantly reduced the risk of drug-induced bradycardia in both pediatric and adult surgical patients (Carron et al., 2017; Hristovska et al., 2017; Liu et al., 2017). Sugammadex was also associated with a significantly reduced risk of PORC and postoperative weakness (Carron et al., 2017; Hristovska et al., 2017). One of the weaknesses in the literature review is the conflicting data pertaining to if sugammadex reduced the incidence of postoperative nausea and vomiting (PONV). One meta-analysis found that sugammadex reduced the incidence of PONV in adult surgical patients, however it expressed its concerns related smaller patient population and limited quality of evidence (Hristovska et al., 2017). Two other meta-analyses did not find a significant reduction in the incidence of PONV

related to sugammadex for both pediatric and adult surgical patients (Carron et al., 2017; Liu et al., 2017). Overall, sugammadex has been associated with reducing postoperative weakness and the risk of numerous adverse events, however there is limited evidence to support that sugammadex reduces the risk of PONV.

Sugammadex has also been attributed to ensuring a complete, effective reversal from neuromuscular blockade in patients that are considered at a high risk of postoperative complications with certain comorbidities. Sugammadex effectively reverses neuromuscular blockade in morbidly obese surgical patients and is associated with quicker reversal times, shorter anesthesia time, and higher postoperative saturation (Robertis et al., 2016; Evron et al., 2017). One of the patient populations that is at an increased risk of postoperative respiratory complications includes patients with obstructive sleep apnea, in which sugammadex has been associated with quicker, effective reversal and lower risk of postoperative respiratory risks (Unal et al., 2015). Sugammadex has also been found to effectively reverse patients with end-stage renal failure surgical patients without any incidence of adverse event or recurarization (Souza et al., 2015). Even though the elderly and old-elderly surgical patients have a slightly prolonged recovery times, one study found that sugammadex has been shown to effectively reverse neuromuscular blockade without any documented adverse events (McDonagh et al., 2011). The use of sugammadex has further been attributed to adequate reversal of neuromuscular blockade in patient with liver disease, and is associated with faster recovery times and shorter stay in the PACU (Abdulatif, Lotfy, Mousa, Afifi, & Yassen, 2018).

Sugammadex can be used to reverse a rapid sequence induction dose of rocuronium effectively, and limit the risk of a CVCI event. Sugammadex administered 3 minutes after 1.2

mg/kg dose of rocuronium significantly increased recovery from deep neuromuscular blockade compared to a rapid-sequence induction dose of succinylcholine by 4 minutes (Chambers et al., 2010). The authors further identified that full reversal from a large dose of rocuronium only took a mean time of 2.2 minutes in which other reversal strategies are contraindicated, in which can eliminate the life-threatening risk of a CVCI scenario.

There is a current gap in the literature related to the cost effectiveness of reversal with sugammadex as the sole reversal agent for rocuronium and vecuronium induced neuromuscular blockade. This is a complicated topic because the cost of the reversal agent is not the only factor to deduce what the overall cost is for the patient, in which sugammadex is more expensive per dose compared to neostigmine. However, sugammadex has been found to significantly reduce the risk of postoperative adverse events and reduced time in the operating rooms and postoperative care units, which theoretically can reduce the overall care costs. In certain singles site studies, it has been advised that the use of sugammadex for patients with morbid obesity or obstructive sleep apnea can reduce the total cost to the patient by reducing the risk of complications and time in recovery (Robertis et al., 2016; Unal et al., 2015). There is limited research to support that sugammadex is cost effective and reduces overall surgical costs for all surgical patients in every clinical scenario, primarily due to the increased in cost per reversal dose.

Overall, sugammadex has been found to reverse the effects of neuromuscular blockade more effectively and timely compared to currently used reversal agents. Sugammadex has been associated with the safe use reversing rapid sequence induction doses of rocuronium which can lead to a significant reduction in the incidences of CVCI scenarios. It has been effective at

reversing neuromuscular blockade in high risk patient populations, which includes patients with morbid obesity, obstructive sleep apnea, advanced age, cardiovascular disease, chronic renal failure, chronic liver failure, and neuromuscular disease. Furthermore, sugammadex has been correlated with fewer perioperative adverse effects compared to current reversal practices.

METHODS

Design

This project was guided by the KTA framework and LCT resulting in the development of a CPG for sugammadex. Recommendations were adapted from the literature search and evaluated by anesthesia providers using the Appraisal of Guidelines for Research & Evaluation II (AGREE II) Instrument to assess for quality and validity (Brouwers et al., 2010). The My AGREE PLUS, an electronic version of the assessment tool, was used. The CPG and results were made available to the designated facility for implementation.

Setting and Participants

This project took place in the Phoenix-Metropolitan area with a convenience sample of volunteer anesthesia providers currently practicing. The AGREE II Instrument recommends that the guideline is assessed by at least two appraisers and preferably four to increase reliability (Brouwers et al., 2010). Four anesthesia providers (N=4) were included in the My AGREE PLUS evaluation process. Each of the participants were experienced Certified Nurse Anesthetists (CRNAs) whom are currently using sugammadex in their practice. To reduce the risk of a biased evaluation, all participants that were either full-time employees at the designated facility or were involved with the development of the CPG were strictly excluded from the evaluation process.

Key Stakeholder Involvement

Key anesthesia stakeholders at the designated facility were also involved in this DNP project. One key stakeholder at the designated facility, a CRNA with experience on the Banner University Anesthesia Consensus Committee, was selected to provide expert opinion to help tailor the guideline to the facility. Key leaders were also involved in this DNP Project, including the Director of Anesthesia and the Chief CRNA. Both leaders expressed unprecedented support to the use of sugammadex in the perioperative phase, however the facility has been cautious in accepting sugammadex due to perceived increase of reversal costs. To clarify, a total of three stakeholders, one anesthesiologist and two CRNAs, were involved throughout the development of this DNP project and provided pertinent organizational insight to enhance applicability.

Guideline Development

The development of the CPG on the regulated use of sugammadex followed the AGREE II framework, which is a systematic process to improve the quality of practice guidelines. The AGREE Reporting checklist was utilized during the development phase of the CPG (Appendix C). The AGREE Reporting checklist provides specific reporting criteria for each domain and question that the AGREE II tool assesses. The intent is to assist clinicians to ensure completeness and transparency when reporting CPGs. The current recommendations on the use of sugammadex were summarized in an easy to understand and follow guideline. An anesthesia provider championed the CPG development in collaboration with the author to ensure that current practices and applicability of the recommendations are considered. The anesthesia provider had valuable pharmacy input on facilitators and barriers to sugammadex implementation. This information was vital for the interdisciplinary applicability of the

developed CPG. It is highly recommended that content area experts are included, such as anesthesia providers, in the development and appraisal of guidelines to increase both quality of evaluation and comprehension of the CPG (Brouwers et al., 2010). This CPG incorporated evidence based recommendations on adequately reversing patients that have received either rocuronium or vecuronium induced neuromuscular blockade that results in patient scenarios of CVCI, inadequately reversed neuromuscular blockade, premature termination of surgical procedure, or high risk of postoperative complications (Appendix D).

Level of Evidence

The level of evidence and grade of recommendations were evaluated during the developing phase to ensure transparency. The level of evidence was determined using the Levels of Evidence for Therapeutic Studies (Figure 4). The level of evidence is taken into account when grading the specific recommendations on the CPG (Burns, Rohrich, & Chung, 2011). The use of systematic review of RCTs is the highest level of evidence, with the use of case series and expert opinion at the lowest level (Burns, Rohrich, & Chung, 2011). After the level of evidence is quantified, the principle investigator (PI) was able to determine the strength or lack thereof of the recommended intervention. The grading of the recommendations was accomplished using an adaption of the Grade Practice Recommendations (Figure 5).

Level	Type of evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow confidence interval)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual cohort study (including low quality RCT)
2C	"Outcomes" research; Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual case-control studies
4	Case series (and poor quality cohort and case-control studies)
5	Expert opinion; case report or clinical example; or evidence based on physiology

FIGURE 4. Adaptation of levels of evidence for therapeutic studies.

Grade	Descriptor	Qualifying Evidence	Implications for Practice
A	Strong recommendation	Level I evidence or consistent findings from multiple studies of levels II, III, or IV	Clinicians should follow strong recommendation unless clear or compelling rationale for an alternative approach is present
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role
D	Option	Level V evidence; little or no systematic empirical evidence	Clinicians should consider all options in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role

FIGURE 5. Adaptation of grade practice recommendations.

Tools

he CPG development underwent the AGREE II framework, which is a systematic tool to improve the variability in the quality of practice guidelines (Brouwers et al., 2010). The AGREE II Instrument was utilized for appraisal of the practice guidelines. The AGREE Research Trust

provided valuable online training, references, and free downloads for the appraisers. The website's address is https://www.agreetrust.org/

AGREE II

The AGREE Instrument was first established to create a generic tool to assess the process of guideline development and evaluate quality. The goal of the tool is to ensure that only the highest quality CPGs are implemented into practice, which aims at helping providers develop policy and system-related decisions. The AGREE Instrument was first developed in 2003 by the AGREE Collaboration to describe the three components of quality in a CPG, which includes addressing any biases, internal and external validity, and realistic implementation into practice (Brouwers et al., 2010). The AGREE II Instrument is intended for use by numerous stakeholder groups, which includes healthcare providers, guideline developers, policy makers, and educators (Brouwers et al., 2010). Healthcare providers are able to use the AGREE II Instrument to assess newly developed practice guidelines prior to adopting them into clinical practice. It is designed for CPGs at the local, regional, or national organizational levels pertaining to any clinical specialty within any step of the healthcare continuum (Brouwers et al., 2010). The instrument has since been refined to improve its' usability, validity, and reliability. In order to meet the three components, they created a 23-item tool that evaluated six separate quality domains of newly established practice guidelines (Appendix D). The six domains include (1) the scope and practice, (2) stakeholder involvement, (3) rigor of development, (4) clarity of presentation, (5) applicability, and (6) editorial independence. As well the AGREE II tool establishes two final overall assessment items that guide the appraiser to identify overall judgements of the CPG (Brouwers et al., 2010).

Domain 1. Scope and purpose. The authors included items 1-3 in this domain which is concerned with the overall aim of the CPG, the specific health questions, and the target population. The overall goal of the CPG should be clearly identified in detail and related to the clinical problem associated with the targeted patient population. The CPG should clearly establish the expected benefits or outcomes associated with applications of the practice guidelines. The CPG should identify exactly which patient population is included under the guidelines, and exclude populations if relevant (Brouwers et al., 2010).

Domain 2. Stakeholder involvement. The authors included items 4-6 in this domain which focuses on if the guideline was developed by appropriate stakeholders and if it represents the intended users' views pertaining to the recommendations. The developer(s) should include professionals that are relevant to the clinical problem. The preferences of the target population should be considered during the development of the CPG. The target users or providers should be clearly labeled (Brouwers et al., 2010).

Domain 3. Rigor of development. The authors included items 7-14 in this domain which pertains to the process used to gather and synthesize current evidence and methods to formulate recommendations. It should be relevant that a systematic method was used for searching the current evidence based recommendations. The authors should clearly identify criteria for evidence selection, strengths and limitations, methods of formulation, externally reviewed by experts, and a procedure for updating the CPG as needed (Brouwers et al., 2010).

Domain 4. Clarity of presentation. The authors included items 15-17 in this domain which relates to the language, structure, and format of the CPG. The guidelines should provide clear and unambiguous recommendations. The CPG should be well organized and easy to follow

process. Any different options for management, such as drug dosing, should be clearly labeled (Brouwers et al., 2010).

Domain 5. Applicability. The authors included items 18-21 in this domain that relates to perceived barriers and facilitators to implementation, strategies to increase uptake by providers, and resource implications needed for application. There should be an inclusion of advice on how the guidelines can be implemented into practice and overcome perceived barriers. Educational presentation will be included to provide assistance. The CPG should also present criteria for monitoring the outcomes after implementation (Brouwers et al., 2010).

Domain 6. Editorial independence. The authors included items 22-23 in this domain which is concerned with biases associated with the formulation of recommendations and competing interests. There should be no concern pertaining to funding bodies that have influence the content provided in the CPG. Any competing interests of CPG development should be clearly discussed and recorded (Brouwers et al., 2010).

Overall Guideline Assessment

The authors included an overall guideline assessment to identify overall judgements of the appraisers. The appraiser is asked first to rate the overall quality of the CPG based upon their clinical expertise. The second question identifies if they would recommend this guideline for local implementation (Brouwers et al., 2010).

Process and Data Analysis

The My AGREE PLUS tool is an electronic version of the AGREE II Instrument which allows participants to appraise the practice guideline online. The My AGREE PLUS is freely available to the public to complete and track current appraisals. Prior to evaluating the CPG, the

appraisers first underwent an AGREE II Overview tutorial, which provided an avatar guided overview of the AGREE II Instrument that takes approximately 10 minutes to complete. Appraisers were provided a copy of the AGREE II Instrument that provides instructions for completing the CPG evaluation. Further, appraisers were recommended to complete an AGREE II Practice Exercise to improve the standardization of scoring. Each appraiser signed and dated a confirmation of their AGREE II training. Depending upon the length and structure of the CPG, the actual CPG evaluation is estimated to take an average of 1.5 hours for each appraiser. Each item on the AGREE II tool is rated on a 7-point scale, 1 being strongly disagree and 7 being strongly agree. The final product from the assessment tool provided combined calculated quality scores for each domain that helped determine the recommended use of the CPG (Brouwers et al., 2010). The anesthesia consultant and PI determined that a domain score of 70% or greater should be indicative of a high quality domain. The overall scoring of each domain identifies the CPG's overall quality.

The CPG was evaluated by four (n=4) independent appraisers to increase its' reliability (Brouwers et al., 2010). Each appraiser was provided access to the AGREE II Overview Tutorial and AGREE II Practice Exercise to improve the standardization of scoring. The appraisers also received the CPG via email as a PDF file. Further, the appraisers were provided instructions on how to create an account on My AGREE PLUS and navigate the website. All information was provided by September 17, 2018. The PI coordinated the group appraisal through the My AGREE PLUS electronic tool, and the group name was titled "DNP Project: Sugammadex Clinical Practice Guideline." The appraisers were allotted two weeks to assess the CPG and

provide valuable insight to its quality. All four appraisals were completed and results compiled on September 30, 2018.

Ethical Considerations

This DNP project did not include patient participants or vulnerable populations. The University of Arizona Institutional Review Board determined this project was not considered human research (Appendix F). In regards for the principle of respect for persons, all participants were provided disclose information via email and signed an Appraiser Training Confirmation form (Appendix I). The email included a full disclosure to the nature and purpose of the project. Pertaining to the beneficence principle, this project focused on updating the current standard of practice to include the safest delivery of anesthesia. Justice principle was accomplished through impartial and volunteer participation.

RESULTS

The AGREE II results provide each appraisers' score per item, inputted comments per item, cumulative domain scores as percentages, overall assessment scores, and if the appraiser would recommend the CPG (Brouwers et al., 2010). The quantitative results provided by the AGREE II Instrument can be found in Appendix E. The scores were further uploaded into an organized table format (Table 2).

TABLE 2. *Seven-point AGREE II score calculator*.

Seven-point AGREE II Score Calculator					
You must fill in ALL of the Question ratings from an appraiser for the Domain score to be accurate. **Note: Please use the AGREE II User's Manual for full instructions.*					
Total # of Appraisers	**Appraiser**				
4	***1***	***2***	***3***	***4***	
Domain 1 - Scope and Purpose					
Q1 - The overall objective(s) of the guideline is (are) specifically described.	7	7	7	7	28
Q2 - The health question(s) covered by the guideline is (are) specifically described.	7	7	7	7	28
Q3 - The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.	7	7	7	7	28
	21	21	21	21	**84**
			Domain 1 Score for 4 Appraiser(s):		100%
Domain 2 - Stakeholder Involvement					
Q4 - The guideline development group includes individuals from all relevant professional groups.	6	7	7	7	27
Q5 - The views and preferences of the target population (patients, public, etc.) have been sought.	7	7	7	7	28
Q6 - The target users of the guideline are clearly defined.	6	7	7	5	25
	19	21	21	19	**80**
			Domain 2 Score for 4 Appraiser(s):		94%

TABLE 2 – *Continued*

Seven-Point AGREE II Score Calculator

Domain 3 - Rigour of Development					
Q7 - Systematic methods were used to search for evidence.	7	7	6	7	27
Q8 - The criteria for selecting the evidence are clearly described.	7	7	7	7	28
Q9 - The strengths and limitations of the body of evidence are clearly described.	7	7	6	7	27
Q10 - The methods for formulating the recommendations are clearly described.	7	7	6	7	27
Q11 - The health benefits, side efects, and risks have been considered in formulating the recommendations.	7	7	6	7	27
Q12 - There is an explicit link between the recommendations and the supporting evidence.	7	7	6	7	27
Q13 - The guideline has been externally reviewed by experts prior to its publication.	7	7	7	7	28
Q14 - A procedure for updating the guideline is provided.	7	7	7	7	28
	56	56	51	56	**219**
			Domain 3 Score for 4 Appraiser(s):		97%
Domain 4 - Clarity of Presentation					
Q15 - The recommendations are specific and unambiguous.	7	7	7	7	28
Q16 - The different options for management of the condition or health issue are clearly presented.	7	7	6	7	27
Q17 - Key recommendations are easily identifiable	7	7	6	7	27
	21	21	19	21	**82**
			Domain 4 Score for 4 Appraiser(s):		97%
Domain 5 - Applicability					
Q18 - The guideline describes facilitators and barriers to its application.	7	7	7	7	28
Q19 - The guideline provides advice and/or tools on how the recommendations can be put into practice.	7	7	7	7	28
Q20 - The potential resource implications of applying the recommendations have been considered.	7	7	7	7	28
Q21 - The guideline presents monitoring and/or auditing criteria.	7	7	6	7	27
	28	28	27	28	**111**
			Domain 5 Score for 4 Appraiser(s):		99%
Domain 6 - Editorial Independence					
Q22 - The views of the funding body have not influenced the content of the guideline.	7	7	6	7	27
Q23 - Competing interests of guideline development group members have been recorded and addressed.	7	7	7	7	28
	14	14	13	14	**55**
			Domain 6 Score for 4 Appraiser(s):		98%
Overall Guideline Assessment					
1. Rate the overall quality of this guideline. *Scoring: 1(Least Quality) - 7(Highest Quality)*	7	7	7	6	
2. I would recommend this guideline for use. *Scoring: "Yes", "Yes, with modifications", "No"*	Yes	Yes	Yes	Yes	

The combined, calculated domain scores for each of the six domains were 100%, 94%, 97%, 97%, 99%, and 98% respectively. The six domain scores are independent of each other and are calculated separately. Each domain score achieved the 70% quality threshold that was predetermined for a high quality domain (Brouwers et al., 2010). The overall assessment of the CPG's quality received a combined score of 96%. Each appraiser (N=4) recommended the guideline for clinical use without any modifications.

One of the advantages with using the My AGREE PLUS electronic tool is that it provides comments from the appraiser. The comments enhance clarity to the quantitative scores, however they are not considered separate results. The comments included in the AGREE II Instrument are not deemed qualitative measures but are only utilized by the appraiser to clarify their numerical scoring. Leaving a comment after assessing an item is strictly optional, in which Appraiser 3 and Appraiser 4 did not include comments in their evaluation process. Further, there were no comments recorded for Domain 4, Clarity of Presentation, or Domain 6, Editorial Independence.

Comments were recorded for Domain 1, Scope and Purpose, which included items 1 through 3. Pertaining to item 1, Appraiser 2 vocalized that the cost of glycopyrrolate and neostigmine was similar to cost of sugammadex at their institution. Pertaining to item 3, Appraiser 2 determined that the target population was "well described."

Comments were recorded for Domain 2, Stakeholder Involvement, which included items 4 through 6. Pertaining to item 4, Appraiser 1 highlighted the potential benefit of including a pharmacist for development of the guideline. Pertaining to item 6, Appraiser 1 and Appraiser 2 thought the target users of the guideline could be expanded to include postoperative care unit

nurses, critical care medicine physicians, and critical care nurses. Further, Appraiser 2 did not appreciate the term Physician Anesthesiologist in identifying the target users of this guideline.

Comments were recorded for Domain 3, Rigour of Development, which included items 7 through 14. Pertaining to item 9, Appraiser 2 expressed concern with the lack of a definition to the term recurarization, in which potential users of the guideline could be confused to its meaning. Pertaining to item 12, Appraiser 2 deemed the key recommendations as "current and well-documented". Pertaining to item 14, Appraiser 2 expressed concern that 5 years for updating the guideline may be too long.

Comments were recorded for Domain 5, Applicability, which included items 18 through 21. Pertaining to item 19, Appraiser 1 determined that the algorithm was "very well made, concise, and easy to follow" and Appraiser 2 stated that they "loved the algorithm… very clear/easily utilized".

DISCUSSION

The results provided through the AGREE II Instrument have deemed this CPG as high quality. Each domain score achieved and surpassed the predetermined quality threshold of 70%. All the appraisers of the CPG recommended its guideline and key components for clinical use without modifications. The key recommendations identified clinical scenarios that deemed the necessity of sugammadex administration; including 1) as a rescue therapy in the rare but life-threatening "cannot-ventilate, cannot-intubate" situation, 2) for residual, moderate, or deep neuromuscular blockade, in which the patient would either be at risk for inadequate reversal with standard reversal agents or any further administration of standard reversal agents is contraindicated, and 3) to ensure complete reversal for patients with significant comorbidities

that are at risk for postoperative complications. Including patients with neuromuscular disease, respiratory disease, cardiovascular disease, hepatic dysfunction, advanced age, morbid obesity, and obstructive sleep apnea. The overall quality of the CPG received a combined score of 96%, with only one appraiser not rating a perfect score.

Given the scores and appraiser comments, Domain 2, Stakeholder Involvement, proved to be the weakest domain. The overall score of 94% was the lowest combined domain score. It still achieved the quality threshold, however there were a couple factors that could have improved its overall score. There was a concern identified that a pharmacist was not included in the CPG development team. The inclusion of a pharmacist stakeholder in the development process would have enhanced a significant facilitator for the guideline's overall implementation. As well, there were concerns to the predetermined target users of the guideline. It could be beneficial to include intraoperative and postoperative care nurses whom provided valuable assessments of the patient's condition. However, the inclusion of critical care medicine physicians and critical care nurses would not be indicated for this CPG due to its focus on the perioperative phase.

Dissemination Plan

The goal of the CPG is to translate the best evidence into the best practice. Key leaders at the designated facility were sought out during the guideline development process and after the AGREE II evaluation to disseminate the results. The key leaders included the Medical Director of Anesthesia and the Chief CRNA; in which they both provide valuable influence that can change the current practice at the site and have significant relationships in place to overcome organizational barriers.

An oral presentation was provided to the leaders pertaining to the CPG and the AGREE II results, in which they both deemed the guideline as high quality. After the presentation, a questionnaire was utilized to evaluate the overall intent to change and implement into practice (Appendix G). This questionnaire was separate from the AGREE II results above, and was developed to determine intent to change. They both identified that the rationale for developing a CPG for the use of sugammadex was clear and there is a significant need for it at their institution. They both determined that the key recommendations were clear, suitable for their patient population, provided more benefit than harm, and were interpreted correctly with current literature. Further, they agreed with implementing the key recommendations as stated without modifications. Both leaders denied that the CPG would be difficult to apply, and agreed that the majority of their colleagues would support the change. They both identified that the key recommendations reflected a more effective approach for improving patient outcomes than currently used practices. When asked if the CPG should be approved as a practice guideline, both leaders selected “strongly agreed”. When asked if they would use the CPG in their own practice if it had previously been approved as a practice guideline, both leaders selected “strongly agree”. When asked if they would apply the recommendation to their own patients if it had previously been approved as a practice guideline, both leaders selected “strongly agree”. Both key leaders expressed their intent to change and implement this CPG into practice.

The only organizational barrier that currently stands is pharmacy’s previous resistance to purchasing sugammadex and including it within the facility’s pharmaceutical formulary. The pharmacist whom controls the pharmacy budget has stated their concerns that the reversal per patient is more expensive with sugammadex compared to the neostigmine/glycopyrrolate

mixture. Both leaders have developed a respectable relationship with pharmacy and are planning a meeting to reevaluate the decision to incorporate sugammadex. Both leaders selected “neither agree or disagree” when asked if the CPG was too expensive to apply, due to their perspective that it could significantly reduce postoperative complications, time in the operating room, time in the PACU, and costly intensive care admissions.

Overall, the anesthesia leaders were able to get sugammadex approved and now on formulary through collaboration with pharmacy. They both deemed that the CPG is of high quality and expressed their intent to integrate it into their anesthesia practice. The results were disseminated to these anesthesia leaders as they comprehend the current facility’s barriers and facilitators and have significant influence on pertinent organizational decisions.

The results will be further presented during the AZANA Annual Sun & Fun Conference in March, 2019 and the NMANA Nurse Anesthesia Conference in September, 2019. This will include a presentation of the CPG and results to anesthesia providers around the state.

Strengths, Weaknesses and Limitations

This DNP project has had many potential strengths that supported its development process and acceptance by key stakeholders. Most importantly, the literature that was used to support the effectiveness of sugammadex was of high level evidence that supported strong recommendations. The synthesis of evidence and majority studies used in this DNP project included random controlled trials, systematic reviews, and meta-analyses. These study designs are considered of the highest level of evidence (Burns, Rohrich, & Chung, 2011). Further, the use of sugammadex is gaining much momentum in current anesthesia practice which enabled the PI to find enthusiastic volunteers. The AGREE II Instrument used in this DNP project is

identified as one of the most credible assessment tools for appraising CPGs, in that it has been cited in well over 600-hundred different publications (Brouwers et al., 2010). The PI was able to recruit the ideal amount of appraisers for this DNP project, in that the AGREE II team encourages at least two but preferably four participants (Brouwers et al., 2010). The four volunteer appraisers are anesthesia experts whom are currently using sugammadex in practice and were not biased, full-time employees at the designated facility. Lastly, the PI of this DNP project was able to implore the strong rapport established with key anesthesia leaders at the facility, in which they have expressed their strong intent to change and implement.

The fact that the CPG was developed by a single PI whom had limited influence at the designated facility was the most recognized weakness to this DNP project. As identified in the AGREE II results, the lowest scoring aspect in the assessment tool was the stakeholder involvement. The domain entailed the item of including all relevant professional groups in the guideline development group, in which the inclusion of a pharmacist could have enhanced the overall quality of the CPG. However, the appraiser that highlighted the need to incorporate a pharmacist determined that it was also "highly appropriate" to seek out expert anesthesia providers for the development phase.

One of the limitations to the use of the AGREE II Instrument is that the assessment tool cannot guarantee appropriate or improved patient outcomes based solely on rigor of development (Brouwers et al., 2010). Simply using the AGREE II Instrument does not ensure that the appraised CPG is flawless, however it does increase the probability of producing high quality recommendations. Another limitation is that the DNP project was developed for a single institution, and may have limited representativeness. Some healthcare organizations may have no

barriers resisting the use of sugammadex in anesthesia practice, and a CPG that identifies which clinical scenarios are appropriate for sugammadex is unwarranted.

Incorporation of DNP Essentials

The eight DNP essentials were incorporated in this DNP project to see it to fruition.

- *DNP I*: Application of scientific underpinnings to practice was clearly completed through the inclusion of LCT and the KTA Framework in the theoretical section of this DNP project.
- *DNP II:* Application of organizational and systems leadership for quality improvement and systems thinking was accomplished through engagement of key leaders to help facilitate implementation.
- *DNP III*: Application of clinical scholarship and analytical methods of evidence-based practice was the bases for the entire methodology of this DNP project in that it aimed to progress current evidence into current practice by developing a CPG.
- *DNP IV*: Application of information systems/technology and patient care technology for the improvement and transformation of heath care was clearly completed with utilization of the My AGREE PLUS electronic tool which allows appraisers to assess CPGs online and provided combined quality results.
- *DNP V*: Application of healthcare policy for advocacy in healthcare was applied by adapting the CPG for regulated use of sugammadex due to the current economic status of the healthcare organization.
- *DNP VI*: Application of interprofessional collaboration for improving patient and population health outcomes was completed by engaging CRNAs and physician

anesthesiologists in this DNP project, as well as addressing the need to reach out to pharmacy stakeholders.

- *DNP VII*: Application of clinical prevention and population health for improving the nation's health had limited involvement in this DNP project, however the overall aim was to reduce postoperative patient risks and improve the perioperative population's health outcomes.
- *DNP VIII*: Application of advanced practice competencies was represented with the PI's advanced knowledge pertaining to the neuromuscular junction physiology, advanced pharmacotherapeutics, and background knowledge to the issue of recurarization. The eight DNP essentials were clearly recognized throughout this DNP project.

The eight DNP essentials were clearly recognized throughout this DNP project.

Conclusion

The use of sugammadex is revolutionizing how anesthesia providers are reversing neuromuscular blockade. Sugammadex implementation compared to currently used practices has the capability to reduce postoperative patient risks and complications. A current and evidence-based CPG was developed with the input from key stakeholders. The presented CPG in this project will provide guidance to anesthesia providers on the appropriate use of sugammadex, and will help propel change forward for the designated facility. DNP prepared APRNs are in place to make significant changes in healthcare and ensure that evidence-based CPGs correlate to best practices. This DNP project was able to develop a CPG that produced quality-driven, evidence-based recommendations that promotes applicability and implores intent to change.

APPENDIX A:

AGREE II INSTRUMENT

Domain 1: Scope and Practice
1. The overall objective (s) of the guideline(s) is specifically described.
2. The health question (s) covered by the guideline is (are) specifically described.
3. The population to whom the guideline is meant to apply is specifically described.
Domain 2: Stakeholder Involvement
4. The guideline development group includes individuals from all relevant professional groups.
5. The views and preferences of the target population have been sought.
6. The target users of the guideline are clearly defined.
Domain 3: Rigour of Development
7. Systematic methods were used to search for evidence.
8. The criteria for selecting the evidence are clearly described.
9. The strengths and limitations of the body of evidence are clearly described.
10. The methods for formulating the recommendations are clearly described.
11. The health benefits, side effects, and risks have been considered in formulating the recommendations.
12. There is an explicit link between the recommendations and the supporting evidence.
13. The guideline has been externally reviewed by experts prior to its publication.
14. A procedure for updating the guideline is provided.
Domain 4: Clarity of Presentation
15. The recommendations are specific and unambiguous.
16. The different options for management of the condition or health issue are clearly presented.
17. Key recommendations are easily identifiable.
Domain 5: Applicability
18. The guideline describes facilitators and barriers to its application.
19. The guideline provides advice and/or tools on how the recommendation can be put into practice.
20. The potential resource implications of applying the recommendation have been considered.
21. The guideline presents monitoring and/or auditing criteria.
Domain 6: Editorial Independence
22. The views of the funding body have not influenced the content of the guideline.
23. Competing interests of guideline development group members have been recorded and addressed.
Overall Guideline Assessment
1. Rate the overall quality of the guideline.
2. I would recommend this guideline for use.

APPENDIX B:

AGREE II SCORE SHEET

AGREE II Score Sheet

Domain	Item	AGREE II Rating						
		1 *Strongly Disagree*	**2**	**3**	**4**	**5**	**6**	**7** *Strongly Agree*
Scope and purpose	1. The overall objective(s) of the guideline is (are) specifically described.							
	2. The health question(s) covered by the guideline is (are) specifically described.							
	3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described.							
Stakeholder involvement	4. The guideline development group includes individuals from all the relevant professional groups.							
	5. The views and preferences of the target population (patients, public, etc.) have been sought.							
	6. The target users of the guideline are clearly defined.							
Rigor of development	7. Systematic methods were used to search for evidence.							
	8. The criteria for selecting the evidence are clearly described.							
	9. The strengths and limitations of the body of evidence are clearly described.							
	10. The methods for formulating the recommendations are clearly described.							
	11. The health benefits, side effects and risks have been considered in formulating the recommendations.							
	12. There is an explicit link between the recommendations and the supporting evidence.							
	13. The guideline has been externally reviewed by experts prior to its publication.							
	14. A procedure for updating the guideline is provided.							
Clarity of presentation	15. The recommendations are specific and unambiguous.							
	16. The different options for management of the condition or health issue are clearly presented.							
	17. Key recommendations are easily identifiable.							
Applicability	18. The guideline describes facilitators and barriers to its application.							
	19. The guideline provides advice and/or tools on how the recommendations can be put into practice.							
	20. The potential resource implications of applying the recommendations have been considered.							
	21. The guideline presents monitoring and/ or auditing criteria.							
Editorial independence	22. The views of the funding body have not influenced the content of the guideline.							
	23. Competing interests of guideline development group members have been recorded and addressed.							
Overall Guideline Assessment	1. Rate the overall quality of this guideline.	**1** *Lowest possible quality*	**2**	**3**	**4**	**5**	**6**	**7** *Highest possible quality*
Overall Guideline Assessment	2. I would recommend this guideline for use.	*Yes*	*Yes, with modifications*					*No*

APPENDIX C:

AGREE REPORTING CHECKLIST

AGREE Reporting Checklist
2016

This checklist is intended to guide the reporting of clinical practice guidelines.

CHECKLIST ITEM AND DESCRIPTION	REPORTING CRITERIA	Page #
DOMAIN 1: SCOPE AND PURPOSE		
1. OBJECTIVES *Report the overall objective(s) of the guideline. The expected health benefits from the guideline are to be specific to the clinical problem or health topic.*	☐ Health intent(s) (i.e., prevention, screening, diagnosis, treatment, etc.) ☐ Expected benefit(s) or outcome(s) ☐ Target(s) (e.g., patient population, society)	
2. QUESTIONS *Report the health question(s) covered by the guideline, particularly for the key recommendations.*	☐ Target population ☐ Intervention(s) or exposure(s) ☐ Comparisons (if appropriate) ☐ Outcome(s) ☐ Health care setting or context	
3. POPULATION *Describe the population (i.e., patients, public, etc.) to whom the guideline is meant to apply.*	☐ Target population, sex and age ☐ Clinical condition (if relevant) ☐ Severity/stage of disease (if relevant) ☐ Comorbidities (if relevant) ☐ Excluded populations (if relevant)	
DOMAIN 2: STAKEHOLDER INVOLVEMENT		
4. GROUP MEMBERSHIP *Report all individuals who were involved in the development process. This may include members of the steering group, the research team involved in selecting and reviewing/rating the evidence and individuals involved in formulating the final recommendations.*	☐ Name of participant ☐ Discipline/content expertise (e.g., neurosurgeon, methodologist) ☐ Institution (e.g., St. Peter's hospital) ☐ Geographical location (e.g., Seattle, WA) ☐ A description of the member's role in the guideline development group	
5. TARGET POPULATION PREFERENCES AND VIEWS *Report how the views and preferences of the target population were sought/considered and what the resulting outcomes were.*	☐ Statement of type of strategy used to capture patients'/publics' views and preferences (e.g., participation in the guideline development group, literature review of values and preferences) ☐ Methods by which preferences and views were sought (e.g., evidence from literature, surveys, focus groups) ☐ Outcomes/information gathered on patient/public information ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
6. TARGET USERS *Report the target (or intended) users of the guideline.*	☐ The intended guideline audience (e.g. specialists, family physicians, patients, clinical or institutional leaders/administrators) ☐ How the guideline may be used by its target audience (e.g., to inform clinical decisions, to inform policy, to inform standards of care)	

DOMAIN 3: RIGOUR OF DEVELOPMENT		
7. SEARCH METHODS *Report details of the strategy used to search for evidence.*	☐ Named electronic database(s) or evidence source(s) where the search was performed (e.g., MEDLINE, EMBASE, PsychINFO, CINAHL) ☐ Time periods searched (e.g., January 1, 2004 to March 31, 2008) ☐ Search terms used (e.g., text words, indexing terms, subheadings) ☐ Full search strategy included (e.g., possibly located in appendix)	
8. EVIDENCE SELECTION CRITERIA *Report the criteria used to select (i.e., include and exclude) the evidence. Provide rationale, where appropriate.*	☐ Target population (patient, public, etc.) characteristics ☐ Study design ☐ Comparisons (if relevant) ☐ Outcomes ☐ Language (if relevant) ☐ Context (if relevant)	
9. STRENGTHS & LIMITATIONS OF THE EVIDENCE *Describe the strengths and limitations of the evidence. Consider from the perspective of the individual studies and the body of evidence aggregated across all the studies. Tools exist that can facilitate the reporting of this concept.*	☐ Study design(s) included in body of evidence ☐ Study methodology limitations (sampling, blinding, allocation concealment, analytical methods) ☐ Appropriateness/relevance of primary and secondary outcomes considered ☐ Consistency of results across studies ☐ Direction of results across studies ☐ Magnitude of benefit versus magnitude of harm ☐ Applicability to practice context	
10. FORMULATION OF RECOMMENDATIONS *Describe the methods used to formulate the recommendations and how final decisions were reached. Specify any areas of disagreement and the methods used to resolve them.*	☐ Recommendation development process (e.g., steps used in modified Delphi technique, voting procedures that were considered) ☐ Outcomes of the recommendation development process (e.g., extent to which consensus was reached using modified Delphi technique, outcome of voting procedures) ☐ How the process influenced the recommendations (e.g., results of Delphi technique influence final recommendation, alignment with recommendations and the final vote)	
11. CONSIDERATION OF BENEFITS AND HARMS *Report the health benefits, side effects, and risks that were considered when formulating the recommendations.*	☐ Supporting data and report of benefits ☐ Supporting data and report of harms/side effects/risks ☐ Reporting of the balance/trade-off between benefits and harms/side effects/risks ☐ Recommendations reflect considerations of both benefits and harms/side effects/risks	
12. LINK BETWEEN RECOMMENDATIONS AND EVIDENCE *Describe the explicit link between the recommendations and the evidence on which they are based.*	☐ How the guideline development group linked and used the evidence to inform recommendations ☐ Link between each recommendation and key evidence (text description and/or reference list) ☐ Link between recommendations and evidence summaries and/or evidence tables in the results section of the guideline	

13. EXTERNAL REVIEW *Report the methodology used to conduct the external review.*	☐ Purpose and intent of the external review (e.g., to improve quality, gather feedback on draft recommendations, assess applicability and feasibility, disseminate evidence) ☐ Methods taken to undertake the external review (e.g., rating scale, open-ended questions) ☐ Description of the external reviewers (e.g., number, type of reviewers, affiliations) ☐ Outcomes/information gathered from the external review (e.g., summary of key findings) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations (e.g., guideline panel considered results of review in forming final recommendations)	
14. UPDATING PROCEDURE *Describe the procedure for updating the guideline.*	☐ A statement that the guideline will be updated ☐ Explicit time interval or explicit criteria to guide decisions about when an update will occur ☐ Methodology for the updating procedure	
DOMAIN 4: CLARITY OF PRESENTATION		
15. SPECIFIC AND UNAMBIGUOUS RECOMMENDATIONS *Describe which options are appropriate in which situations and in which population groups, as informed by the body of evidence.*	☐ A statement of the recommended action ☐ Intent or purpose of the recommended action (e.g., to improve quality of life, to decrease side effects) ☐ Relevant population (e.g., patients, public) ☐ Caveats or qualifying statements, if relevant (e.g., patients or conditions for whom the recommendations would not apply) ☐ If there is uncertainty about the best care option(s), the uncertainty should be stated in the guideline	
16. MANAGEMENT OPTIONS *Describe the different options for managing the condition or health issue.*	☐ Description of management options ☐ Population or clinical situation most appropriate to each option	
17. IDENTIFIABLE KEY RECOMMENDATIONS *Present the key recommendations so that they are easy to identify.*	☐ Recommendations in a summarized box, typed in bold, underlined, or presented as flow charts or algorithms ☐ Specific recommendations grouped together in one section	
DOMAIN 5: APPLICABILITY		
18. FACILITATORS AND BARRIERS TO APPLICATION *Describe the facilitators and barriers to the guideline's application.*	☐ Types of facilitators and barriers that were considered ☐ Methods by which information regarding the facilitators and barriers to implementing recommendations were sought (e.g., feedback from key stakeholders, pilot testing of guidelines before widespread implementation) ☐ Information/description of the types of facilitators and barriers that emerged from the inquiry (e.g., practitioners have the skills to deliver the recommended care, sufficient equipment is not available to ensure all eligible members of the	

	population receive mammography) ☐ How the information influenced the guideline development process and/or formation of the recommendations	
19. IMPLEMENTATION ADVICE/TOOLS *Provide advice and/or tools on how the recommendations can be applied in practice.*	☐ Additional materials to support the implementation of the guideline in practice. For example: ▫ Guideline summary documents ▫ Links to check lists, algorithms ▫ Links to how-to manuals ▫ Solutions linked to barrier analysis (see Item 18) ▫ Tools to capitalize on guideline facilitators (see Item 18) ▫ Outcome of pilot test and lessons learned	
20. RESOURCE IMPLICATIONS *Describe any potential resource implications of applying the recommendations.*	☐ Types of cost information that were considered (e.g., economic evaluations, drug acquisition costs) ☐ Methods by which the cost information was sought (e.g., a health economist was part of the guideline development panel, use of health technology assessments for specific drugs, etc.) ☐ Information/description of the cost information that emerged from the inquiry (e.g., specific drug acquisition costs per treatment course) ☐ How the information gathered was used to inform the guideline development process and/or formation of the recommendations	
21. MONITORING/ AUDITING CRITERIA *Provide monitoring and/or auditing criteria to measure the application of guideline recommendations.*	☐ Criteria to assess guideline implementation or adherence to recommendations ☐ Criteria for assessing impact of implementing the recommendations ☐ Advice on the frequency and interval of measurement ☐ Operational definitions of how the criteria should be measured	
DOMAIN 6: EDITORIAL INDEPENDENCE		
22. FUNDING BODY *Report the funding body's influence on the content of the guideline.*	☐ The name of the funding body or source of funding (or explicit statement of no funding) ☐ A statement that the funding body did not influence the content of the guideline	
23. COMPETING INTERESTS *Provide an explicit statement that all group members have declared whether they have any competing interests.*	☐ Types of competing interests considered ☐ Methods by which potential competing interests were sought ☐ A description of the competing interests ☐ How the competing interests influenced the guideline process and development of recommendations	

APPENDIX D:

CLINICAL PRACTICE GUIDELINE

Perioperative Administration of Sugammadex: A Clinical Practice Guideline

Report Date: September 15, 2018

Scope and Purpose

Objectives

This guideline provides certified nurse anesthetists and physician anesthesiologists evidence-based methods for reversal of rocuronium or vecuronium induced neuromuscular blockade with the administration of sugammadex with the goal of optimizing patient safety. Sugammadex is a more expensive reversal agent compared to conventional anticholinesterase agents and has the potential to increase drug expenditure. This guideline provides evidence-based clinical indications for the use of sugammadex, as it has been found to provide a faster and more efficient reversal. Secondary objectives include introducing evidence-based key recommendations for diagnostic values of level of blockade, prevention of postoperative complications, and treatment for high risk patient populations.

Questions

What are the most appropriate clinical indications for the use of sugammadex in the perioperative phase? What patient populations are at risk for postoperative complications related to residual paralysis?

Target Population

This guideline is intended for adult patient populations, age 18 years old or greater, male and female, who received either rocuronium or vecuronium intraoperatively. Patients excluded from this guideline include those aged 17 years or younger, have severe renal impairment, have a known sensitivity to sugammadex, or received a different neuromuscular blocking agent.

Intended Users

Physician Anesthesiologists

Certified Registered Nurse Anesthetists

Student Registered Nurse Anesthetists

Pharmacists

Key Recommendations

Sugammadex demonstrates the capability of reversing neuromuscular blockade more timely and effectively [2,3,7,10]. It has shown clinical advantages for patients with preexisting comorbidities and reducing risks of postoperative respiratory, cardiac, and recurarization complications [2, 5, 7, 10]. However, due to current cost implications and limited evidence supporting cost effectiveness, the use of sugammadex should be restricted for specific situations only.

Sugammadex reversal of rocuronium or vecuronium induced neuromuscular blockade in the following indications:

1. **As a rescue therapy in the rare but life-threatening "cannot-ventilate, cannot-intubate" situation [4].**

Aggregate Evidence Quality	**Grade A**
Benefits	Effective reversal of profound neuromuscular blockade within 3 minutes after sugammadex administration. All other standard reversal agents are contraindicated with the depth of blockade. Negates significant risks of hypoventilation, hypoxemia, and respiratory arrest related to a "cannot-ventilate, cannot-intubate" emergency situation.
Risk, Harm, Costs	Risk of adverse effects of pharmacological intervention; cost for high dose sugammadex.
Benefits-Harms Assessment	Preponderance of benefit
Level of Evidence	1A
Descriptor	**Strong Recommendation**

2. **For residual, moderate, or deep neuromuscular blockade, in which the patient would either be at risk for inadequate reversal with standard reversal agents or any further administration of standard reversal agents is contraindicated [2,3,7].**

Aggregate Evidence Quality	**Grade A**
Benefits	Effective reversal of neuromuscular blockade at any depth within 3 minutes after sugammadex administration. Reduces the risk of postoperative recurarization and correlated postoperative complications. Current standard reversal agents are contraindicated for deep neuromuscular blockade or after maximum doses already administrated with residual paralysis.
Risk, Harm, Costs	Risk of adverse effects of pharmacological intervention; cost for sugammadex.
Benefits-Harms Assessment	Preponderance of benefit
Level of Evidence	1A
Descriptor	**Strong Recommendation**

3. To ensure complete reversal for patients with significant comorbidities that are at risk for postoperative complications. Including patients with neuromuscular disease [11], respiratory disease [2,5], cardiovascular disease [2], hepatic dysfunction [1], advanced age [8], morbid obesity [5,6], and obstructive sleep apnea [6,10].

Aggregate Evidence Quality	Grade A
Benefits	Effective reversal of neuromuscular blockade within 3 minutes after sugammadex administration. Ensure unequivocal reversal of paralysis for high risk patient populations. Negates significant risks of respiratory, cardiovascular, or global adverse events
Risk, Harm, Costs	Risk of adverse effects of pharmacological intervention; cost for sugammadex.
Benefits-Harms Assessment	Preponderance of benefit
Level of Evidence	1B
Descriptor	**Strong Recommendation**

Supporting Evidence

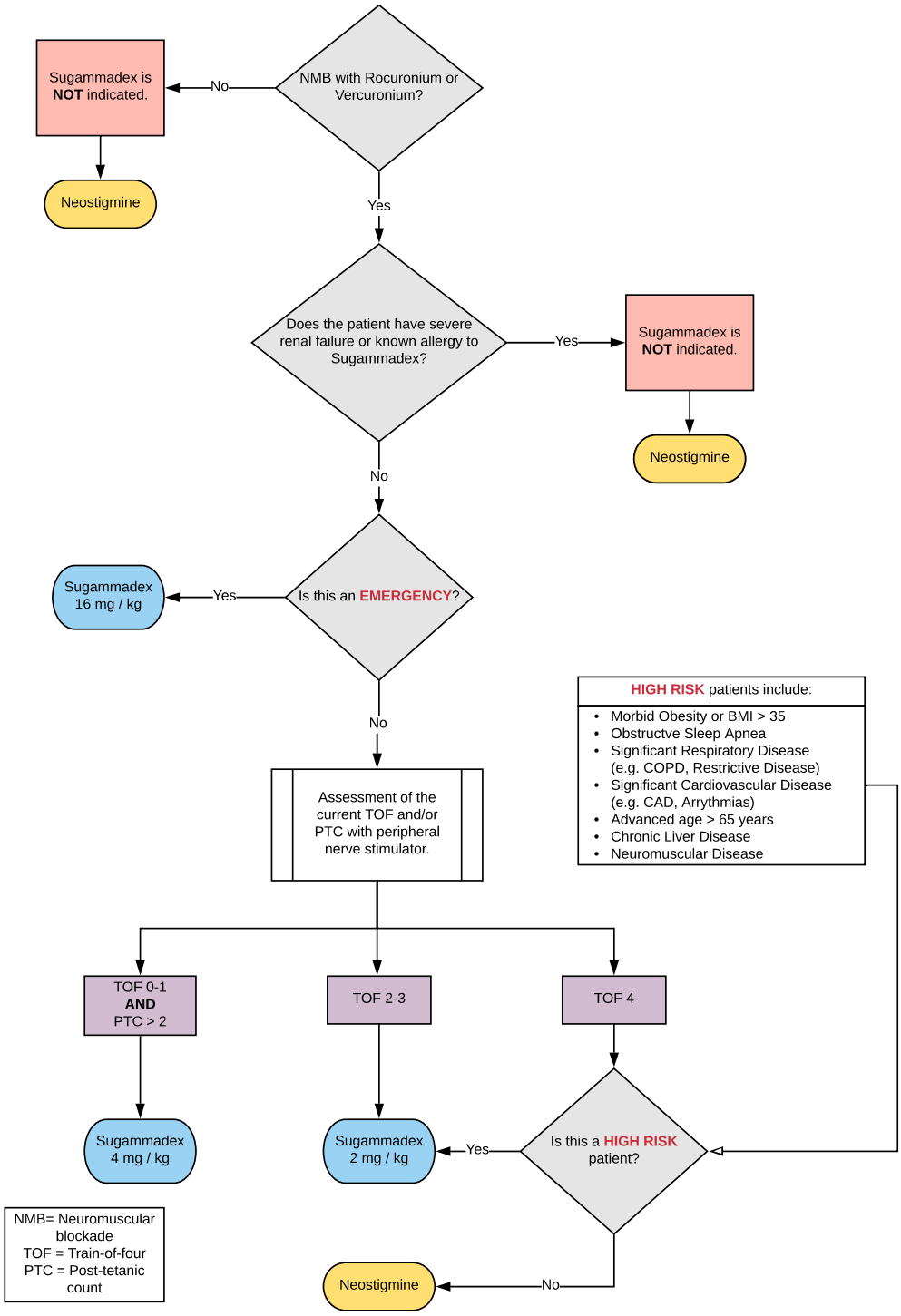
Published cost-analysis evaluations reveal that there may be some significant resource savings due to reduced postoperative adverse events and less time stayed in the operating rooms and postoperative care units, however there is limited applicability due to changes in pharmaceutical costs and variety of surgical specialties (1-11).

1. Abdulatif, M., Lotfy, M., Mousa, M., Afifi, M., & Yassen, K. (2018). Sugammadex antagonism of rocuronium-induced neuromuscular blockade in patients with liver cirrhosis undergoing liver resection: a randomized controlled study. *Minerva Anestesiologica*.
2. Carron, M., Zarantonello, F., Tellaroli, P., & Ori, C. (2016). Efficacy and safety of sugammadex compared to neostigmine for reversal of neuromuscular blockade: a meta-analysis of randomized controlled trials. *Journal of Clinical Anesthesia, 35*, 1-12.
3. Carron, M., Zarantonello, F., Lazzarotto, N., Tellaroli, P., & Ori, C. (2017). Role of sugammadex in accelerating postoperative discharge: A meta-analysis. *Journal of Clinical Anesthesia*, 38-44.
4. Chambers, D., Paulden, M., Paton, F., Heirs, M., Duffy, S., Hunter, J., Sculpher, M., & Woolacott, N. (2010). Sugammadex for reversal of neuromuscular block after rapid sequence intubation: a systematic review and economic assessment. *British Journal of Anaesthesia, 105*(5), 568-575.
5. Evron, S., Abelansky, Y., Ezri, T., & Izakson, A. (2017). Respiratory events with sugammadex vs. neostigmine following laparoscopic sleeve gastrectomy: a prospective pilot study assessing neuromuscular reversal strategies. *Romanian Journal of Anaesthesia and Intensive Care, 24*, 111-114.
6. Hafeez, K., Tuteja, A., Singh, M., Wong, D., Nagappa, M., Chung, F., & Wong, J. (2018). Postoperative complications with neuromuscular blocking drugs and/or reversal agents in obstructive sleep apnea patients: a systematic review. *BMC Anesthesiology, 18*(1).

7. Hristovska, A., Duch, P., Allingstrup, M., & Afshari, A. (2017). The comparative efficacy and safety of sugammadex and neostigmine in reversing neuromuscular blockade in adults. A Cochrane systematic review with meta-analysis and trial sequential analysis. *Anaethesia*.
8. McDonagh, D., Benedict, P., Kovac, A., Drover, D., Brister, N., Morte, J., & Monk, T. (2011). Efficacy, safety, and pharmacokinetics of sugammadex for the reversal of rocuronium-induced neuromuscular blockade in elderly patients. *The Journal of the American Society of Anesthesiologists, 114*(2), 318-329.
9. Robertis, E., Marinosci, G., Romano, G., Piazza, O., Iannuzzi, M., Cirillo, F., et al. (2016). The use of sugammadex for bariatric surgery: analysis of recovery time from neuromuscular blockade and possible economic impact. *ClinicoEconomics and Outcomes Research*, 317-322.
10. Unal, D., Baran, I., Mutlu, M., Ural, G., Akkaya, T., & Ozlu, O. (2015). Comparison of Sugammadex versus Neostigmine Costs and Respiratory Complications in Patients with Obstructive Sleep Apnoea. *Turkish Journal of Anaesthesiology and Reanimation*, 387-395.
11. Vymazal, T., Krecmerova, M., Bicek, V., & Lishke, R. (2015). Feasibility of full and rapid neuromuscular blockade recovery with sugammadex in myasthenia gravis patients undergoing surgery - a series of 117 cases. *Therapeutics and Clinical Risk Management*, 1593-1596.

Sugammadex Prescribing Information	
Monitoring Criteria	Intraoperative monitoring: document the neuromuscular blocking agent used (rocuronium or vecuronium) and assessment with peripheral nerve stimulator prior to sugammadex administration. • Profound blockade: absent train-of-four and post tetanic count • Deep blockade: absent train-of-four with 1 to 2 post-tetanic counts • Standard blockade: train-of-four greater than 2 twitches Postoperative monitoring: document reversal agent used and dose. Continue facility standard monitoring, and appropriate measures for the specific comorbidities and surgical procedure.
Dose	Profound reversal (emergency): 16 mg/kg Deep reversal: 4 mg/kg Standard reversal: 2 mg/kg
Administration	Give as a single bolus injection, within 10 seconds, into an existing intravenous line.
Precautions	Not recommended for use in pediatric patients or patients with severe renal disease. Patient with hypersensitivity to sugammadex is at risk of anaphylaxis, continue to monitor for an appropriate period of time post administration. Risk of marked bradycardia within 3 min of administration, monitor for hemodynamic changes and treat with anticholinergic is severe bradycardia is observed.
Merck. (2015). *Sugammadex Full Prescribing Information.* New Jersey: Merck Sharp & Dohme Corp.	

Implementation Algorithm



Methods

Search Methods and Criteria Selection

Scientific evidence was utilized in the development of this guideline. Search of electronic databases included PubMED, CINAHL, and Cochrane Library. Key search terms were included sugammadex, neostigmine, neuromuscular blockade, obesity, geriatrics, liver disease, renal disease, sleep apnea, rapid sequence induction, safety, and efficacy. Criteria for inclusion consisted of recent publication after 2010, peer-reviewed, full text availability, and English language. Study designs considered included meta-analyses, systematic reviews, and random controlled trials.

Strength of Evidence

The level of evidence was first evaluated and considered when grading each recommendation. The figures below were utilized for the determination of strength of evidence.

Level	Type of evidence
1A	Systematic review (with homogeneity) of RCTs
1B	Individual RCT (with narrow confidence interval)
1C	All or none study
2A	Systematic review (with homogeneity) of cohort studies
2B	Individual cohort study (including low quality RCT)
2C	"Outcomes" research; Ecological studies
3A	Systematic review (with homogeneity) of case-control studies
3B	Individual case-control studies
4	Case series (and poor quality cohort and case-control studies)
5	Expert opinion; case report or clinical example; or evidence based on physiology
Burns, P., Rohrich, R., & Chung, K. (2011). The Levels of Evidence and their role in Evidence-Based Medicine. *Plastic and Reconstructive Surgery, 128*(1), 305-310.	

Grade	Descriptor	Qualifying Evidence	Implications for Practice
A	Strong recommendation	Level I evidence or consistent findings from multiple studies of levels II, III, or IV	Clinicians should follow strong recommendation unless clear or compelling rationale for an alternative approach is present
B	Recommendation	Levels II, III, or IV evidence and findings are generally consistent	Generally, clinicians should follow a recommendation but should remain alert to new information and sensitive to patient preferences
C	Option	Levels II, III, or IV evidence, but findings are inconsistent	Clinicians should be flexible in their decision-making regarding appropriate practice, although they may set bounds on alternatives; patient preference should have a substantial influencing role
D	Option	Level V evidence; little or no systematic empirical evidence	Clinicians should consider all options in their decision making and be alert to new published evidence that clarifies the balance of benefit versus harm; patient preference should have a substantial influencing role
Burns, P., Rohrich, R., & Chung, K. (2011). The Levels of Evidence and their role in Evidence-Based Medicine. *Plastic and Reconstructive Surgery, 128*(1), 305-310.			

External Review and Updating Procedure

External peer review was completed by an anesthesia provider not associated with the guideline development or application. Purpose is to determine quality and clarity, gather feedback, and disseminate results. External peer review was completed by Sarah Torabi, DNP, CRNA. The guideline will undergo internal peer review every five years for newly published literature to support or dissuade current recommendations.

Stakeholder Involvement

The guideline and algorithm was developed by Timothy Markle, SRNA from the University of Arizona. The intended goal was to encourage and implement sugammadex availability at a healthcare facility in the Phoenix Metropolitan area. Key anesthesia personnel provided valuable clinical and institutional insight for this guideline development. The preference of the target population was considered with the overall goal to increase patient safety in the postoperative phase.

Facilitators/Barriers to Implementation

This guideline was developed with the input and feedback from key stakeholders at Mountain Vista Medical Center. All required resources, such as peripheral nerve stimulator, are currently available to the anesthesia personnel. Cost implications to pharmaceutical budget will be the single most pertinent barrier of implementation.

Funding/Conflict of Interest

This guideline was developed as the project of a Doctor of Nursing Practice student. There was no funding required for this project. All work produced by the author is editorially independent and free from competing interests.

Disclaimer

Great effort has been provided in the preperation of this guideline. Nonetheless, any person intending to implement or apply these evidence-based recommendations is expected to use indepenedint clinical judgement in context to each disticnt clinical circumstance or seek out supervision from a qualified clinician.

APPENDIX E:

AGREE II APPRAISAL SCORES

Domain 1	Domain 2	Domain 3	Domain 4	Domain 5	Domain 6	OA 1	OA 2
100%	94%	97%	97%	99%	98%	96%	Yes - 4, Yes with modifications - 0, No - 0

Domain 1. Scope and Purpose				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2
Item 1	7	7	7	7
Item 2	7	7	7	7
Item 3	7	7	7	7
Domain 2. Stakeholder Involvement				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2
Item 4	6	7	7	7
Item 5	7	7	7	7
Item 6	6	7	7	5
Domain 3. Rigour of Development				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2
Item 7	7	7	6	7
Item 8	7	7	7	7
Item 9	7	7	6	7
Item 10	7	7	6	7
Item 11	7	7	6	7
Item 12	7	7	6	7
Item 13	7	7	7	7
Item 14	7	7	7	7
Domain 4. Clarity of Presentation				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2
Item 15	7	7	7	7
Item 16	7	7	6	7
Item 17	7	7	6	7
Domain 5. Applicability				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2

Item 18	7	7	7	7
Item 19	7	7	7	7
Item 20	7	7	7	7
Item 21	7	7	6	7
Domain 6. Editorial Independence				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2
Item 22	7	7	6	7
Item 23	7	7	7	7
Overall Assessment				
	Appraiser 1	Appraiser 4	Appraiser 3	Appraiser 2
OA1	7	7	7	6

Created online at www.agreetrust.org 30 September 2018

APPENDIX F:

THE UNIVERSITY OF ARIZONA INSTITUTIONAL REVIEW BOARD (IRB)

DETERMINATION OF HUMAN RESEARCH FORM

THE UNIVERSITY OF ARIZONA
Research, Discovery & Innovation

Human Subjects Protection Program

1618 E. Helen St.
P.O.Box 245137
Tucson, AZ 85724-5137
Tel: (520) 626-6721
http://rgw.arizona.edu/compliance/home

Date:	July 20, 2018
Principal Investigator:	Timothy Stephen Markle
Protocol Number:	1807773939
Protocol Title:	DEVELOPMENT OF A CLINICAL PRACTICE GUIDELINE FOR THE USE OF SUGAMMADEX
Determination:	Human Subjects Review not Required

Documents Reviewed Concurrently:

Data Collection Tools: *AGREE II Instrument.pdf*
Data Collection Tools: *Appraiser's email and disclosure.docx*
HSPP Forms/Correspondence: *Advisor Confirmation Email.pdf*
HSPP Forms/Correspondence: *DNP Sugammadex Determination of Human Research.pdf*
Other Approvals and Authorizations: *APOA site authorization.docx*

Regulatory Determinations/Comments:

- Not Research as defined by 45 CFR 46.102(d): As presented, the activities described above do not meet the definition of research cited in the regulations issued by U.S. Department of Health and Human Services which state that "research means a systematic investigation, including research development, testing and evaluation, designed to contribute to generalizable knowledge."

The project listed above does not require oversight by the University of Arizona.

If the nature of the project changes, submit a new determination form to the Human Subjects Protection Program (HSPP) for reassessment. Changes include addition of research with children, specimen collection, participant observation, prospective collection of data when the study was previously retrospective in nature, and broadening the scope or nature of the study activity. Please contact the HSPP to consult on whether the proposed changes need further review.

The University of Arizona maintains a Federalwide Assurance with the Office for Human Research Protections (FWA #00004218).

APPENDIX G:

DISSEMINATION RESULTS

Please select the appropriate demographic category that most accurately descrines you.

Type of anesthesia provider:			Years practiced in current role:					
☐ SRNA	☒ CRNA	☐ Physician	☐ <5	☐ 5-10	☐ 11-15	☒ 16-20	☐ 21-25	☐ 25+

	Yes	No	Unsure
1. Are you responsible for the care of patients for whom this draft guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.	☒	☐	☐

If you answered "*No*" or "*Unsure*", there is no need to answer or return this questionnaire. If you answered "*Yes*", please answer the questions below and return to **Tim Markle SRNA**

	Strongly agree	Neither agree or disagree	Strongly disagree
2. The rationale for developing a guideline is clear.	☒	☐	☐
3. There is a need for a guideline on this topic.	☒	☐	☐
4. The literature search is relevant and complete (e.g., no key evidence was missed nor any included that should not have been) in this draft guideline.	☒	☐	☐
5. I agree with the methodology used to summarize the evidence included in this draft guideline.	☒	☐	☐
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.	☒	☐	☐
7. The draft recommendations in this report are clear.	☒	☐	☐
8. I agree with the draft recommendations as stated.	☒	☐	☐
9. The draft recommendations are suitable for the patients for whom they are intended.	☒	☐	☐
10. The draft recommendations are too rigid to apply to individual patients.	☐	☐	☒
11. When applied, the draft recommendations will produce more benefits for patients than harms.	☒	☐	☐
12. The draft guideline presents options that will be acceptable to patients.	☒	☐	☐
13. To apply the draft recommendations will require reorganization of services/care in my practice setting. MUST CHANGE PHARMACY Support	☒	☐	☐
14. To apply the draft guideline recommendations will be technically challenging.	☐	☐	☒
15. The draft guideline recommendations are too expensive to apply.	☐	☒	☐
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.	☒	☐	☐
17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.	☒	☐	☐
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☒	☐	☐
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☒	☐	☐
20. I would feel comfortable if my patients received the care recommended in the draft guideline.	☒	☐	☐
21. This draft guideline should be approved as a practice guideline.	☒	☐	☐
22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.	☒	☐	☐
23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.	☒	☐	☐

Adapted From: Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, Fervers B, Graham ID, Grimshaw J, Hanna S, Littlejohns P, Makarski J, Zitzelsberger L for the AGREE Next Steps Consortium. AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Can Med Assoc J. 2010.* Available online May 31, 2018. doi:10.1503/cmaj.090449

Please select the appropriate demographic category that most accurately descrines you.

Type of anesthesia provider:			Years practiced in current role:					
☐ SRNA	☐ CRNA	☐ Physician	☐ <5	☐ 5-10	☐ 11-15	☐ 16-20	☐ 21-25	☐ 25+

1. Are you responsible for the care of patients for whom this draft guideline report is relevant? This may include the referral, diagnosis, treatment, or follow-up of patients.	Yes ☐	No ☐	Unsure ☐
If you answered "*No*" or "*Unsure*", there is no need to answer or return this questionnaire. If you answered "*Yes*", please answer the questions below and return to **Tim Markle SRNA**			
	Strongly agree	Neither agree or disagree	Strongly disagree
2. The rationale for developing a guideline is clear.	☐	☐	☐
3. There is a need for a guideline on this topic.	☐	☐	☐
4. The literature search is relevant and complete (e.g., no key evidence was missed nor any included that should not have been) in this draft guideline.	☐	☐	☐
5. I agree with the methodology used to summarize the evidence included in this draft guideline.	☐	☐	☐
6. The results of the evidence described in this draft guideline are interpreted according to my understanding of the evidence.	☐	☐	☐
7. The draft recommendations in this report are clear.	☐	☐	☐
8. I agree with the draft recommendations as stated.	☐	☐	☐
9. The draft recommendations are suitable for the patients for whom they are intended.	☐	☐	☐
10. The draft recommendations are too rigid to apply to individual patients.	☐	☐	☐
11. When applied, the draft recommendations will produce more benefits for patients than harms.	☐	☐	☐
12. The draft guideline presents options that will be acceptable to patients.	☐	☐	☐
13. To apply the draft recommendations will require reorganization of services/care in my practice setting.	☐	☐	☐
14. To apply the draft guideline recommendations will be technically challenging.	☐	☐	☐
15. The draft guideline recommendations are too expensive to apply.	☐	☐	☐
16. The draft guideline recommendations are likely to be supported by a majority of my colleagues.	☐	☐	☐
17. If I follow the draft guideline recommendations, the expected effects on patient outcomes will be obvious.	☐	☐	☐
18. The draft guideline recommendations reflect a more effective approach for improving patient outcomes than is current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☐	☐	☐
19. When applied, the draft guideline recommendations will result in better use of resources than current usual practice. (If they are the same as current practice, please tick NA). *NA* ☐	☐	☐	☐
20. I would feel comfortable if my patients received the care recommended in the draft guideline.	☐	☐	☐
21. This draft guideline should be approved as a practice guideline.	☐	☐	☐
22. If this draft guideline were to be approved as a practice guideline, I would use it in my own practice.	☐	☐	☐
23. If this draft guideline were to be approved as a practice guideline, I would apply the recommendations to my patients.	☐	☐	☐

Adapted From: Brouwers M, Kho ME, Browman GP, Burgers JS, Cluzeau F, Feder G, Fervers B, Graham ID, Grimshaw J, Hanna S, Littlejohns P, Makarski J, Zitzelsberger L for the AGREE Next Steps Consortium. AGREE II: Advancing guideline development, reporting and evaluation in healthcare. *Can Med Assoc J. 2010.* Available online May 31, 2018. doi:10.1503/cmaj.090449

APPENDIX H:

SITE AUTHORIZATION FORM

Anesthesia Physicians of Arizona
1301 South Crimson Road
Mesa, AZ 85209

June 9, 2018

University of Arizona Institutional Review Board
c/o Office of Human Subjects
1618 E Helen St
Tucson, AZ 85721

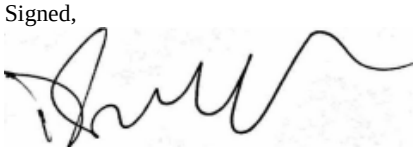
Please note that Mr. Timothy Markle, UA Doctor of Nursing Practice student, has permission of Anesthesia Physicians of Arizona to conduct an evidence-based project for his project, "Development of a Clinical Practice Guideline for the Use of Sugammadex."

Mr. Markle will develop a clinical practice guideline with the input of a CRNA from our anesthesia group. The CRNA will provide expert opinion and valuable organizational insight from Mountain Vista Medical Center. This will include an interview conducted off site as agreed upon from both parties. Mr. Markle's activities will be completed by December 31, 2018.

Mr. Markle has agreed to provide the developed clinical practice guideline and evaluation results upon completion. He has further agreed to present the results to the providers as per organizational determination.

If there are any questions, please contact my office.

Signed,



Dr. Ned Sciortino
Medical Director of Anesthesia

APPENDIX I:

APPRAISER DISCLOSURE EMAIL

Dear Appraiser,

You have been selected to contribute significant insight and expertise for my DNP project, "Development of a Clinical Practice Guideline for the Use of Sugammadex".

The purpose of this project is to identify the current evidence-based recommendations for the reversal of neuromuscular blockade with Sugammadex and develop a high quality clinical practice guideline at the organizational level.

If you choose to take part in this project, you will be asked to appraise the clinical practice guideline for quality and applicability. It will take approximately 10 minutes to complete an AGREE II Overview tutorial and 90 minutes to evaluate the developed clinical practice guideline. There are no foreseeable risks associated with participating in this project and you will receive no immediate benefit from your participation. Evaluation responses are anonymous.

If you choose to participate in the project, participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which you are otherwise entitled. You may withdraw at any time from the project. In addition, you may skip any question that you choose not to answer. By participating, you do not give up any personal legal rights you may have as a participant in this project.

For questions, concerns, or complaints about the project, you may call Timothy Markle BSN, RN, SRNA at (602) 568-3236 or tsmarkle@email.arizona.edu.

Thank you for volunteering and for the time that you have sacrificed.

Sincerely,

Timothy Markle BSN, RN, SRNA
University of Arizona
tsmarkle@email.arizona.edu

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